PB81-117335

Ambient Water Quality Criteria for Asbestos

(U.S.) Environmental Protection Agency
Washington, DC

Oct 80

U.S. Department of Commerce
National Technical Information Service
NTIS

United States
Environmental Protection
Agency

Office of Water
Regulations and Standards
Criteria and Standards Division
Washington DC 20460

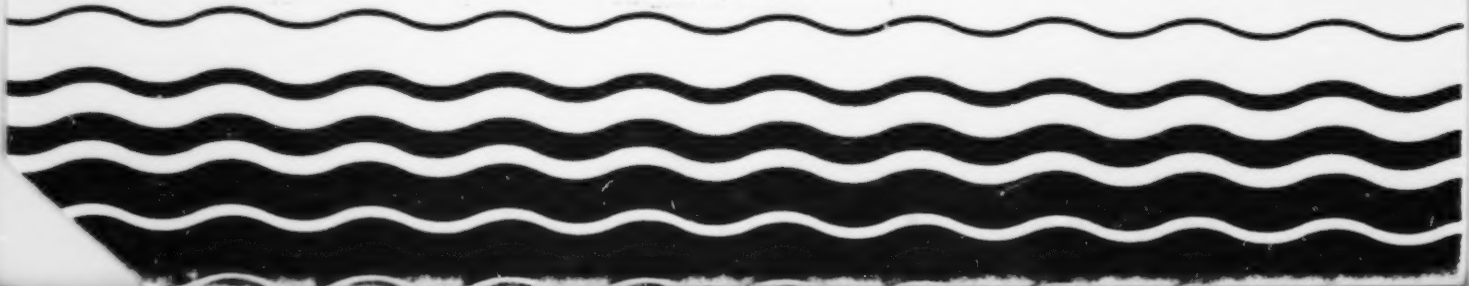
EPA 440/5-80-022
October 1980

PB81-117335

EPA

Ambient Water Quality Criteria for Asbestos

REPRODUCED BY
NATIONAL TECHNICAL
INFORMATION SERVICE
U.S. DEPARTMENT OF COMMERCE
SPRINGFIELD, VA 22161



TECHNICAL REPORT DATA

(Please read Instructions on the reverse before completing)

1. REPORT NO.

2.

3. RECIPIENT'S ACCESSION NO. PB81 117335

4. TITLE AND SUBTITLE
Ambient Water Quality Criteria for:
Asbestos

5. REPORT DATE
October, 1980

6. PERFORMING ORGANIZATION CODE
NTISEPAOWP

7. AUTHOR(S)
Environmental Criteria and Assessment Office

8. PERFORMING ORGANIZATION REPORT NO.
EPA 440/5-80-022

9. PERFORMING ORGANIZATION NAME AND ADDRESS
Office of Water Regulations and Standards
Criteria and Standards Division
U.S. Environmental Protection Agency
Washington, D.C. 20460

10. PROGRAM ELEMENT NO.

11. CONTRACT/GRANT NO.

12. SPONSORING AGENCY NAME AND ADDRESS
Same.

13. TYPE OF REPORT AND PERIOD COVERED

14. SPONSORING AGENCY CODE

15. SUPPLEMENTARY NOTES
Supersedes draft document PB 297 917

16. ABSTRACT

Section 304(A) of the Clean Water Act [33 U.S.C. 1314(A)], requires EPA to publish and periodically update water quality criteria. These criteria are to reflect the latest scientific knowledge on the identifiable effects of pollutants on public health and welfare, aquatic life, and recreation. This report presents water quality criteria for Asbestos. It presents concentration criteria for the protection of freshwater and saltwater aquatic life. It presents 'safe' concentrations for humans, and in the case of suspect or proven carcinogens, gives various levels of incremental cancer risk. A Section 304(A) water quality criterion is a qualitative or quantitative estimate of the concentration of a water constituent or pollutant in ambient waters which, when not exceeded, will ensure a water quality sufficient to protect a specified water use. Under the Act a criterion is a scientific entity, based solely on data and scientific judgment. It does not reflect considerations of economic or technological feasibility nor is it a water quality standard and in itself has no regulatory effect.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group

18. DISTRIBUTION STATEMENT
For Public Release

19. SECURITY CLASS *(This Report)*
Unclassified

20. SECURITY CLASS *(This page)*
Unclassified

21. NO. OF PAGES

22. PRICE

EPA Form 2220-1 (9-73)

AMBIENT WATER QUALITY CRITERIA FOR

ASBESTOS

Prepared By
U.S. ENVIRONMENTAL PROTECTION AGENCY

Office of Water Regulations and Standards
Criteria and Standards Division
Washington, D.C.

Office of Research and Development
Environmental Criteria and Assessment Office
Cincinnati, Ohio

Carcinogen Assessment Group
Washington, D.C.

Environmental Research Laboratories
Corvalis, Oregon
Duluth, Minnesota
Gulf Breeze, Florida
Narragansett, Rhode Island

DISCLAIMER

This report has been reviewed by the Environmental Criteria and Assessment Office, U.S. Environmental Protection Agency, and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

AVAILABILITY NOTICE

This document is available to the public through the National Technical Information Service, (NTIS), Springfield, Virginia 22161.

FOREWORD

Section 304 (a)(1) of the Clean Water Act of 1977 (P.L. 95-217), requires the Administrator of the Environmental Protection Agency to publish criteria for water quality accurately reflecting the latest scientific knowledge on the kind and extent of all identifiable effects on health and welfare which may be expected from the presence of pollutants in any body of water, including ground water. Proposed water quality criteria for the 65 toxic pollutants listed under section 307 (a)(1) of the Clean Water Act were developed and a notice of their availability was published for public comment on March 15, 1979 (44 FR 15926), July 25, 1979 (44 FR 43660), and October 1, 1979 (44 FR 56628). This document is a revision of those proposed criteria based upon a consideration of comments received from other Federal Agencies, State agencies, special interest groups, and individual scientists. The criteria contained in this document replace any previously published EPA criteria for the 65 pollutants. This criterion document is also published in satisifaction of paragraph 11 of the Settlement Agreement in Natural Resources Defense Council, et. al. vs. Train, 8 ERC 2120 (D.D.C. 1976), modified, 12 ERC 1833 (D.D.C. 1979).

The term "water quality criteria" is used in two sections of the Clean Water Act, section 304 (a)(1) and section 303 (c)(2). The term has a different program impact in each section. In section 304, the term represents a non-regulatory, scientific assessment of ecological effects. The criteria presented in this publication are such scientific assessments. Such water quality criteria associated with specific stream uses when adopted as State water quality standards under section 303 become enforceable maximum acceptable levels of a pollutant in ambient waters. The water quality criteria adopted in the State water quality standards could have the same numerical limits as the criteria developed under section 304. However, in many situations States may want to adjust water quality criteria developed under section 304 to reflect local environmental conditions and human exposure patterns before incorporation into water quality standards. It is not until their adoption as part of the State water quality standards that the criteria become regulatory.

Guidelines to assist the States in the modification of criteria presented in this document, in the development of water quality standards, and in other water-related programs of this Agency, are being developed by EPA.

STEVEN SCHATZOW
Deputy Assistant Administrator
Office of Water Regulations and Standards

ACKNOWLEDGEMENTS

Aquatic Life Toxicology

William A. Brungs, ERL-Narragansett
U.S. Environmental Protection Agency

John H. Gentile, ERL-Narragansett
U.S. Environmental Protection Agency

Mammalian Toxicology and Human Health Effects:

William Nicholson (author)
Mt. Sinai School of Medicine

Steven Bayard, CAG
U.S. Environmental Protection Agency

Debdas Mukerjee (doc. mgr.) ECAO-Cin
U.S. Environmental Protection Agency

Roy E. Albert, CAG*
U.S. Environmental Protection Agency

Bonnie Smith (doc. mgr.) ECAO-Cin
U.S. Environmental Protection Agency

Robert Bruce, ECAO-RTP
U.S. Environmental Protection Agency

Gary Chapman, ERL-Corvallis
U.S. Environmental Protection Agency

Robert Carton, OTS
U.S. Environmental Protection Agency

W. Clark Cooper

Patrick Durkin
Syracuse Research Corp.

Michael Flaherty
U.S. Environmental Protection Agency

Alfred Garvin
University of Cincinnati

Thomas J.Haley
National Center for Toxicological Res.

Phillip M. Cook, ERL-Duluth
U.S. Environmental Protection Agency

Si Duk Lee, ECAO-Cin
U.S. Environmental Protection Agency

Richard Lemen
National Inst. for Occupational Safety and Health

Steven D. Lutkenhoff, ECAO-Cin
U.S. Environmental Protection Agency

Gary S. Logsdon, MERL-Cin
U.S. Environmental Protection Agency

James Millette, HERL-Cin
U.S. Environmental Protection Agency

Charles Poreli, OTS
U.S. Environmental Protection Agency

James Rowe, OTS
U.S. Environmental Protection Agency

Jerry F.Stara, ECAO-Cin
U.S. Environmental Protection Agency

Technical Support Services Staff: D.J. Reisman, M.A. Garlough, B.L. Zwayer, P.A. Daunt, K.S. Edwards, T.A. Scandura, A.T. Pressley, C.A. Cooper, M.M. Denessen.

Clerical Staff: C.A. Haynes, S.J. Faehr, L.A. Wade, D. Jones, B.J. Bordicks, B.J. Quesnell, C. Russom, B. Gardiner.

*CAG Participating members: Elizabeth L. Anderson, Larry Anderson, Ralph Arnicar, Steven Bayard, David L. Bayliss, Chao W. Chen, John R. Fowle III, Bernard Haberman, Charalingayya Hiremath, Chang S. Lao, Robert McGaughy, Jeffrey Rosenblatt, Dharm V. Singh, and Todd W. Thorslund.

TABLE OF CONTENTS

Page

Criteria Summary

Introduction A-1

Aquatic Life Toxicology B-1
- Effects B-1
- Summary B-1
- Criteria B-1
- References B-2

Mammalian Toxicology and Human Health Effects C-1
- Introduction C-1
- Exposure C-1
  - Analytical Techniques C-1
  - Ingestion from Water C-13
  - Ingestion from Food C-19
  - Exposure from Drugs C-20
  - Inhalation C-20
- Pharmacokinetics C-28
  - Absorption and Distribution C-28
  - Excretion C-32
- Effects C-32
  - Acute, Subacute, and Chronic Toxicity C-32
  - Teratogenicity C-39
  - Mutagenicity C-38
  - Carcinogenicity-Animal Data C-40
  - Carcinogenicity-Human Data C-60
  - Synergism and/or Antagonism C-90
  - Fiber Size Considerations C-94
- Criterion Formulation C-97
  - Existing Standards and Guidelines C-97
  - Current Levels of Exposure C-98
  - Special Groups at Risk C-99
  - Basis and Derivation of Criteria C-100
- References C-115

Appendix I C-139
Appendix II C-140
Appendix III C-141

CRITERIA DOCUMENT

ASBESTOS

CRITERIA

Aquatic Life

No freshwater organisms have been tested with any asbestiform mineral and no statement can be made concerning acute or chronic toxicity

No saltwater organisms have been tested with any asbestiform mineral and no statement can be made concerning acute or chronic toxicity.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to asbestos through ingestion of water and contaminated aquatic organisms, the ambient water concentration should be zero. The estimated levels which would result in increased lifetime cancer risks of 10^{-5}, 10^{-6}, and 10^{-7} are 300,000 fibers/l, 30,000 fibers/l, and 3,000 fibers/l, respectively. Estimates for consumption of aquatic organisms only, excluding the consumption of water cannot be made.

INTRODUCTION

Asbestos is a broad term applied to numerous fibrous mineral silicates composed of silicon, oxygen, hydrogen, and metal cations such as sodium, magnesium, calcium, or iron. There are two major groups of asbestos, serpentine (chrysotile) and amphibole. Chrysotile is the major type of asbestos used in the manufacture of asbestos products. These products include asbestos cement pipe, flooring products, paper products (e.g., padding), friction materials (e.g., brake linings and clutch facings), roofing products, and coating and patching compounds. In 1975, the total consumption of asbestos in the U.S. was 550,900 metric tons.

Of the 243,527 metric tons of asbestos discharged to the environment, 98.3 percent was discharged to land, 1.5 percent to air, and 0.2 percent to water. Solid waste disposal by consumers was the single largest contribution to total discharges. Although no process water is used in dry mining of asbestos ore, there is the potential for runoff from asbestos waste-tailings, wetmining, and iron ore mining. Mining operations can also contribute substantially to asbestos concentrations in water via air and solid waste contamination. In addition to mining and industrial discharges of asbestos, asbestos fibers, which are believed to be the result of rock outcroppings, are found in rivers and streams.

The chemical composition of different asbestos fibers varies widely and typical formulas are presented in Table 1 (U.S. EPA, 1976). It should be noted that the values obtained from actual chemical analysis of the various fibers also may differ slightly from the typical formulas. Although chrysotile is considered to be a distinct mineral, the five amphibole minerals are each varieties of other minerals (Zoltai and Stout, 1976). These minerals differ from each other both chemically and physically with the exception that

TABLE 1

Typical Formulas for Asbestos Fibers

1. Serpentines	Chrysotile	$Mg_3Si_2O_5(OH)_4$
2. Amphiboles	Amosite	$(Mg,Fe)_7Si_8O_{22}(OH)_2$
	Crocidolite	$Na_2(Mg,Fe)_5Si_8O_{22}(OH)_2$
	Anthophyllite	$(Mg,Fe)_7Si_8O_{22}(OH)_2$
	Tremolite	$Ca_2Mg_5Si_8O_{22}(OH)_2$
	Actinolite	$Ca_2(Mg,Fe)_5Si_8O_{22}(OH)_2$

they all contain silicon and all form fibers when crushed. Good quality asbestos will form fibers with higher ratios of length to width than poorer grades.

The basic crystal form of the amphibole minerals is less complicated than for chrysotile. The basic structure consists of a double silica chain (Si_4O_{11}) that is paired back-to-back with a layer of hydrated cations between the chains (Speil and Leineweber, 1969).

Some typical physical properties of three different mineral forms are presented in Table 2 (Gaze, 1965).

Asbestos minerals, despite a relatively high fusion temperature, are completely decomposed at temperatures of 1,000°C. Both the dehydroxylation temperature and decomposition temperature increase with increased MgO content among the various amphibole species (Speil and Leineweber, 1969).

The solubility product constants for various chrysotile fibers range from 1.0×10^{-11} to 3×10^{-12}. Most materials have a negative surface charge in aqueous systems. However, since chrysotile has a positive (+) charge, it will attract, or be attracted to, most dispersed materials. The highly reactive surface of asbestos causes many surface reactions which are intermediate between simple absorption and a true chemical reaction. The absorption of various materials on the surface of chrysotile supports the premise that the polar surface of chrysotile has a greater affinity for polar molecules (e.g., H_2O,NH_3) than for nonpolar molecules (Speil and Leineweber, 1969).

Of all the asbestos minerals, chrysotile is the most susceptible to acid attack. It is almost completely destroyed within 1 hour in 1 N HCl at 95°C. Amphibole fibers are much more resistant to mineral acids (Lindell, 1972).

TABLE 2

Typical Physical Properties of Chrysotile (White Asbestos), Crocidolite (Blue Asbestos), and Amosite*

	Units	Chrysotile (white asbestos)	Crocidolite	Amosite (blue asbestos)
Approximate diameter of smallest fibers	micron	0.01	0.08	0.1
Specific gravity	-	2.55	3.37	3.45
Average tensile strength	lb/inch^2	3.5×10^5	5×10^5	1.75×10^5
Modulus of elasticity	lb/inch^2	23.5×10^6	27.0×10^6	23.5×10^6

*Source: Gaze, 1965

The resistance of the asbestos fibers to attack by reagents other than acid is excellent up to temperatures of approximately 100°C with rapid deterioration observed at higher temperatures. Chrysotile is completely decomposed in concentrated KOH at 200°C. In general, organic acids have a tendency to react slowly with chrysotile (Speil and Leineweber, 1969).

REFERENCES

Gaze, R. 1965. The physical and molecular structure of asbestos. Ann. N.Y. Acad. Sci. 132: 23.

Lindell, K.V. 1972. Biological effects of asbestos. Int. Agency Res. Cancer, Lyon, France.

Speil, S. and J.P. Leineweber. 1969. Asbestos minerals in modern technology. Environ. Res. 2: 166.

U.S. EPA. 1976. Asbestos: A review of selected literature through 1973 relating to environmental exposure and health effects. EPA-560/2-76-001. U.S. Environ. Prot. Agency, Washington, D.C.

Zoltai, T. and J.H. Stout. 1976. Comments on asbestiform and fibrous mineral fragments relative to Reserve Mining Co. taconite deposits. Prepared for Minnesota Pollut. Control Agency.

Aquatic Life Toxicology

EFFECTS

No appropriate data on the effects of asbestos on aquatic organisms are available at this time. Therefore, no freshwater or saltwater criterion can be derived for asbestos. However, microscopic inorganic particles, analyzed by transmission electron microscopy, have been detected in fish tissues (Batterman and Cook, 1980). Tissue samples obtained from a river with known chrysotile asbestos contamination and lake trout, brook trout, and channel catfish exposed to Lake Superior water contaminated with amphibole fibers have been found to contain mineral fibers identical to those in the water. Muscle tissue concentrations are about one-twelfth of the average water concentrations (by volume) but liver and kidney fiber concentrations are 500 times greater than muscle tissue concentrations.

Summary

The only available data for asbestos and freshwater organisms results from field studies in which chrysotile and amphibole fibers have been found in tissues of fish collected from freshwater with known concentrations of these mineral fibers.

No data are available for saltwater organisms.

CRITERIA

No freshwater organisms have been tested with any asbestiform mineral, and no statement can be made concerning acute or chronic toxicity.

No saltwater organisms have been tested with any asbestiform mineral, and no statement can be made concerning acute or chronic toxicity.

REFERENCES

Batterman, A. R. and P. M. Cook. 1980. A method for the determination of mineral fibers in fish tissues. Paper to be presented at the 13th Ann. Meeting of the Minnesota Chapter of the American Fisheries Society.

ASBESTOS

Mammalian Toxicology and Human Health Effects

INTRODUCTION

Estimating a risk factor for ingestion of asbestos presents significant difficulties. Although gastrointestinal cancer has been linked to occupational exposures in several groups of workers, no definitive data exist on the effects of direct ingestion of asbestos, either in animals or humans. Further, only limited information exists on air exposure levels for those human studies showing excess risk of gastrointestinal cancer and peritoneal mesothelioma. Nevertheless, the most valuable data on risk are those from human inhalation exposures, and these will form the primary basis for a projected criterion.

This document is not an exhaustive review of all asbestos literature nor are all important papers mentioned herein. However, the papers selected are deemed relevant for estimating dose-response relationships.

EXPOSURE

Analytical Techniques

For the purposes of this document asbestos is defined to be chrysotile, crocidolite, fibrous cummingtonite-grunerite including amosite, fibrous tremolite, fibrous actinolite, and fibrous anthophyllite. The fibrosity of the above minerals is ascertained on a microscopic level with fiber defined to be particles with an aspect ratio of 3 to 1 or greater. This definition will apply to fibers of all sizes. Because of the impossibility of relating fibers in any water system to bulk mineral deposits from whence they came, the mineral nature of fibers will generally be determined, when necessary, by electron beam instrumentation (morphology, selected area electron diffraction, and electron microprobe analysis).

The analytical techniques for the measurement of asbestos minerals in air or water samples collected in occupational or general environmental circumstances are time-consuming, and the results are often highly variable. No single method is suitable for all monitoring circumstances. Techniques appropriate for monitoring workplace exposures are unreliable when used to evaluate the much lower environmental concentrations of asbestos, such as those found in water, largely because of the presence of quantities of other inorganic and organic material. Electron microscopic methods used for environmental monitoring are difficult to perform and costly. Reproducible results can be obtained in experienced laboratories if standardized techniques are utilized, careful quality control is maintained, and periodic interlaboratory comparison of results is made. With careful analysis of water, interlaboratory precision can achieve relative standard deviations of 30 to 65 percent (Anderson and Long, 1980; Chopra, 1978), but without standardization intralaboratory variability can be as great as a factor of ten, and interlaboratory variability can exceed two orders of magnitude (Brown, et al. 1976).

Environmental--Water: Considerable effort has taken place in recent years to standardize techniques for the quantitation of mineral fibers in water. All work to date has utilized electron microscopy. The presence of numerous diatom spicules and other nonasbestos fibers in water and the great difficulty of uniquely identifying mineral species or classes by optical microscopy would appear to preclude the use of optical microscopy for even the quantitation of large asbestos fibers in water. With electron microscopy, however, relatively few experimental problems remain, and reproducible results can be obtained by experienced laboratories. The disadvantage of this method is the cost and time of analysis and the limited availability of laboratories for the analysis of samples.

The U.S. EPA has proposed an interim method for the analysis of asbestos in water (Anderson and Long, 1980). From a 1-liter sample, 50 to 500 ml is filtered through 0.1 micron polycarbonate (Nuclepore) filter. A portion of the filter is placed on an electron microscope grid and dissolved by the Jaffe wick method and scanned by transmission electron microscopy at 10,000 to 20,000 magnification. Prior to dissolution, the flat polycarbonate filters are coated with carbon which serves to enmesh the collected material and to reduce losses during dissolution of the filter material by chloroform. Twenty grid squares or 100 fibers are counted. The identification of fiber type is by morphology for chrysotile and by selected area electron diffraction for amphiboles. No attempt is made to determine the amphibole mineral species. If necessary, this can be done using energy-dispersive X-ray analysis of each fiber. All individual fibers (length greater than three times width), irrespective of length are counted in the grid squares scanned. The fibers in large clumps, though, are not counted individually. For surveillance of large numbers of water systems, the procedures serve to identify those with significant quantities of asbestos present. For water systems with high concentrations of suspended solids, the collected material and filter can be ashed in an activated oxygen furnace, the remaining material resuspended, ultrasonified, and refiltered.

The sensitivity of procedure this is such as to be able to detect about 250,000 fibers/liter (f/l) or less in most drinking water systems without the need for the ashing and resuspension step. Most municipal water systems contain less than 1 mg/l of suspended solids, and thus 200 ml of water can be filtered through a 10 cm^2 filter for analysis. The counting of 20 grid squares as prescribed above, scans 1.3×10^{-3} cm^2 of filter. In this area typical background counts are less than two fibers. Thus, eight fibers counted would establish a detectable level in a given water sample. With 200 ml of water sampled, this corresponds to 250,000 f/l. In water systems having less suspended solids the lower limit of detection is proportionally lower. With systems containing more suspended material similar detection limits can be achieved following the ashing procedure.

A previously used technique of condensation-washing of cellulose acetate Millipore filter pieces on carbon-coated grids using acetone can result in significant losses unless extreme care is taken. Carbon coating of the Millipore filter is ineffective in enmeshing the fibers because many of them are trapped deep within the interstices of the membrane filter. Condensation of acetone on the grid can result in the formation of pools of solvent on the filter which wash away fibers. Losses as great as 80 percent have been reported using this technique (Chatfield, et al. 1978; Beaman and File, 1976; Chopra, 1978).

Eighteen analytical laboratories participated in an American Society for Testing and Materials (ASTM) Task Group study of the measurement of amphibole and chrysotile fibers in water. Table 1 lists the data on the interlaboratory precision that has been obtained by this group in the analysis of both chrysotile and amphibole fibers. The Task Group concluded:

> The transmission electron microscope is the best basic instrument for the analysis, particularly when it is equipped with selected area electron diffraction and energy-dispersive spectroscopy capabilities. The mean fiber concentrations by different groups agree within a factor of two. The interlaboratory reproducibility of 50 percent can be expected in relatively clean water samples unless the concentration is low. In samples with high concentrations of interfering solids, the precision will not be as good. When applied on a broad scale there are variable and significant losses associated with the condensation-washing of samples containing amphibole. The losses are low and less variable when condensation-washing is used to prepare samples containing chrysotile (Chopra, 1978).

TABLE 1

Interlaboratory Precision Obtained in the Analysis of Water Samples for Chrysotile and Amphibole Minerals*

Sample Type	Number of Laboratories Reporting	Mean Fiber Concentration (10^6 fibers of all sizes/l)	Relative Standard Deviation of Analysis (%)
Chrysotile	10	877	35
Chrysotile	9	119	43
Chrysotile	11	59	41
Chrysotile	9	31	65
Chrysotile	9	28	32
Chrysotile	3	25	35
Amphibole	11	139	50
Amphibole	4	95	52
Amphibole	14	36	66

*Source: Anderson and Long, 1980 (see also Chopra, 1978)

Environmental--Air: As with water, the analysis of ambient air samples by optical techniques introduces significant difficulties. First, the quantity of asbestos in ambient air is only a small fraction of the total aerosol. This aerosol contains large quantities of organic and mineral material of various origins, including many fibers other than asbestos. Therefore, enumeration of fibers collected in ambient air may have little relevance to the asbestos material present. In one instance, a comparison of 25 ambient air samples collected in buildings, some of which were contaminated with asbestos, showed no correspondence between concentrations of fibers longer than 5 μm, as determined using optical microscopic techniques, and the total mass of asbestos present, quantitated by electron microscopic methods (Nicholson, et al. 1975). Here, using the National Institute for Occupational Safety and Health (NIOSH) technique, no fiber concentrations measured exceeded 0.03 f/ml, and contributions to the measured filter concentration from other than asbestos fibers were felt to be significant. A review (Duggan and Culley, 1978) of the results of the analysis of six side-by-side ambient air samples by nine laboratories also highlighted the difficulty of using optical microscopy at low asbestos concentrations. They found that intralaboratory variability could exceed a factor of 10 and the results between laboratories could differ by a factor of 100. The possibility exists that optical techniques using petrographic, polarized light microscopes or dispersion staining techniques could produce better results. This has not been investigated, however.

A variety of techniques, each of which utilizes electron microscopy, have been developed for the analysis of asbestos in the ambient air. At the present time, there is less agreement on an ideal method for air analysis than for water analysis. Two general electron microscopic techniques are utilized for the analysis. One involves the collection of asbestos on cellulose acetate (Millipore) or polycarbonate filters (Nuclepore) (Samudra, et al. 1978) and its subsequent transfer to electron microscope grids. For samples collected on cellulose acetate filters, the filter and collected material are ashed, the ash suspended in water, and the suspension filtered through a polycarbonate filter. Such filters are then processed using techniques similar to those used for water and previously discussed (see Water section). Although not well studied, the use of flat-surfaced polycarbonate filters in field situations may lead to losses of particles prior to sample preparation for analysis.

Direct transfer techniques have other limitations. Ambient aerosols are made up of agglomerates of particles with asbestos fibers attached to a variety of other material. Chrysotile asbestos, for example, with a positive surface charge, readily adheres to any of the large number of negatively charged particles, such as clays, in the ambient air. Without dispersal, these agglomerations can result in the asbestos being obscured when viewed by an electron microscope. Further, agglomeration can occur on the filter during the long collection times required to quantitate low concentrations. In many cases, these agglomerates, which usually are of respirable size, contribute the most to the mass of the sample. Also, they may occur so infrequently that a statistically reliable measure of their quantity is difficult to obtain. To obviate these difficulties, techniques have been developed in which collected material and filter are ashed in a low-temperature, activated oxygen furnace. The resulting residue is dispersed by physical means, either through the application of ultrasonic energy or grinding, and is enmeshed in a nitrocellulose or collodian film for mounting on electron microscope grids or is refiltered through a polycarbonate filter. Such "rub-out" methods also involve losses and, as with washing techniques, require skilled development of the process. A significant disadvantage of this procedure is that the initial physical state of the asbestos is altered prior to enumeration. Therefore, information on the fiber size distribution is not available. Only mass concentrations can be determined. (Nicholson, 1971a; Nicholson and Pundsack, 1973).

To date, there has been less interlaboratory agreement in the analysis of air samples than for water sample analysis. In one interlaboratory comparison of samples collected near a road surfaced with serpentinite rock and analyzed for the mass of chrysotile asbestos, intralaboratory differences exceeded two orders of magnitude, and interlaboratory differences for laboratories using different analysis techniques exceeded four orders of magnitude. Fiber counts were similarly variable (U.S. EPA, 1977). On the other hand, relatively good agreement (average relative standard deviation of 25 percent) was achieved by three laboratories in the analysis for amphiboles of 12 samples collected in Silver Bay, Minnesota (U.S. EPA, 1976).

Analysis of amphiboles in air around Lake Superior by the U.S. EPA and the State of Minnesota has been done using a cellulose ester filter for collection. The filter is shipped to the laboratory where it is ashed in a low temperature oxygen-activated furnace. The residue is resuspended and filtered through a polycarbonate filter. Good recovery and low losses are claimed by the investigators (Cook, 1978).

Occupational: In occupational circumstances, the current method of quantitating asbestos air concentrations is to enumerate all fibers longer than 5 μm collected on a specified area of filter, utilizing phase-contrast light microscopy at 400X magnification [National Institute for Occupational Safety and Health (NIOSH), 1972]. Such instrumentation does not allow identification of the fibers according to mineral type nor is it even sufficient to establish if they are organic or mineral in origin. In general, when the principle fiber in an aerosol is known to be asbestos, this presents no problem. However, in some occupational circumstances, as with the use of insulation materials, fibers of various origins are present in the same material, and this can result in overestimates of the actual asbestos concentrations.

The adoption of a 5 µm cutoff for the length of fibers enumerated was imposed by the limitations of light microscopy. It has long been known that fibers longer than 5 µm and visible by phase contrast microscopy represent only a small fraction of the total number of asbestos fibers in the air (Lynch, et al. 1970). This would present no problem were fiber size distributions similar in different circumstances. However, such is not the case. It has been shown, using electron microscopy, that when chrysotile asbestos concentrations in different exposure circumstances are enumerated, the fraction greater than 5 µm may vary by 10-fold (from 0.4 percent of the total number of fibers present to approximately 5.0 percent). When amphibole varieties of asbestos are also considered, the fraction counted can vary more than 100-fold (Nicholson, et al. 1972). Thus, we do not have an accurate yardstick for the quantitation of asbestos air concentration in the workplace. This does not present serious problems when monitoring for standard compliance but complicates comparisons of health effects between various industrial processes such as mining, manufacturing, and end-product use. It also complicates extrapolations of dose-response relationships determined in occupational circumstances to lower concentrations of asbestos measured in the general environment by other techniques. Nevertheless, when assessing exposure in a defined asbestos aerosol, the precision of optical methods can be good. NIOSH (1976) has estimated that a coefficient of variation of about 20 percent can be achieved in the assessment of asbestos concentrations greater than 0.1 f/ml.

Although fiber counts have been utilized for the assessment of occupational asbestos exposure since 1966, in prior years other methods, usually involving total particle counts (fibrous and nonfibrous), were utilized. Some attempts have been made to relate these earlier counts to present day fiber concentrations (Lynch and Ayer, 1966). However, these have been found to depend strongly on the particular asbestos use process, and no universal conversion factor is available that would relate total particle concentrations in a given circumstance with asbestos fiber counts. It is unfortunate that earlier data have limited relevance, since the disease experience that we are seeing today is the result of exposures that took place 20, 30, or more years previously when work conditions may have been considerably different from those currently existing. Thus, dose-response relationships are tenuous and can only be approximate, based upon current data.

Intercomparison of Techniques: All data, scant as they are, that relate asbestos disease to exposure are derived from studies of workers exposed in occupational environments. In these studies, concentrations of fibers longer than 5 μm were determined using optical microscopy or were estimated from optical microscopic measurements of total particulate matter. On the other hand, all current low-level environmental assessments utilize electron microscopic techniques which are not comparable to those used in the workplace since optical techniques do not provide data on the number of fibers less than 5 μm in length. To extrapolate dose-response data obtained in studies of working groups to environmental exposures, it is necessary to establish the relationship between optical fiber counts and mass or total fiber number determined by electron microscopy.

Recent studies have attempted to relate optical fiber counts (fibers > 5 µm) and TEM counts (all EM-countable fibers). An interlaboratory comparison of optical versus EM counts of chrysotile fibers suggested an average relationship between optical counts and TEM counts of 1:1000 (Winer and Cossette, 1979). The samples studied included air samples from six plants (one asbestos-cement, one brake lining, two treating mills, and two textile plants). Lower ratios are expected for amphibole fibers. An analysis by the U.S. EPA (Personal communication, J. Millette) relating optical fiber counts of fibers longer than 5 µm to total fiber counts by transmission electron microscopy gave a ratio of 400 for six samples of asbestos ceiling insulation material (which, however, may contain fibers other than asbestos and were not actual air samples). Other data by Wallingford (1978) suggest a ratio as low as 15 for EM count to optical counts.

Some data exist that relate optical fiber counts (longer than 5 µm) to the total mass of asbestos as determined by electron microscopic techniques or by other weight determinations of collected airborne asbestos fibers. These are listed in Table 2 and provide crude estimates of a conversion factor relating fiber concentrations (f/ml) to airborne asbestos mass ($\mu g/m^3$). The proposed standards for asbestos in Great Britain by the British Occupational Hygiene Society (BOHS) stated that a "respirable" mass of 0.12 mg asbestos/m^3 was equivalent to 2 f/ml (BOHS, 1968). It was not stated how this relationship was determined. However, if it were from magnesium determinations in an aerosol, the weight determination would likely be high because of the presence of other nonfibrous, magnesium-containing compounds in the aerosol. Such was the case in the work of Lynch, et al. (1970), and their values for the conversion factor are undoubtedly overestimates. The data of Rohl, et al. (1976) are likely to be underestimates

TABLE 2

Measured Relationships Between Optical Fiber Counts and Mass of Airborne Chrysotile

Sampling Situation	Fiber[a] Counts (f/ml)	Mass Concentration ($\mu g/m^3$)	Conversion Factors	
			$\frac{\mu g/m^3}{f/ml}$ or $\frac{\mu g}{10^6 f}$	$10^3 f/mg$
Textile factory BOHS (1968) (weight vs. fiber count)	2	120	60	16
Air chamber monitoring Davis, et al. (1978)	1,950	10,000	5	200
Monitoring brake repair work Rohl, et al. (1976) (E.M. mass vs. fiber count)	0.1 to 4.7 (7 samples)	0.1 to 6.6	0.7 to 24[b] mean = 6	170
Textile mill			150[c]	6.7
Friction products mfg.			70[c]	13.9
Pipe mfg. Lynch, et al. (1970)			45[c]	22.5

---

[a] All fiber counts used phase-contrast microscopy and enumerated fibers longer than 5 μm.

[b] Conversion factor may be low due to losses in E.M. processing.

[c] Conversion factor may be high because of overestimate of asbestos mass on the basis of total magnesium.

because of possible losses in the determination of mass by electron microscopy. No data exist on the procedures used to determine the mass of chrysotile in the data presented by Davis, et al. (1978).

The range of 5 to 150 for the conversion factor relating mass concentration to optical fiber concentration is great, and any average value derived from it has a large uncertainty. However, for the purpose of extrapolating to low mass concentrations from fiber count, the geometric mean, 30 $\mu g/m^3/f/ml$, of the above range of conversion factors will be used. The accuracy of this value is felt to be no more than a factor of 5 and this uncertainty severely limits any extrapolation in which it is used. In the case of amosite, the data of Davis, et al. (1978) suggest that a conversion factor of 18 is appropriate. However, since this data yielded lower chrysotile values than all other chrysotile estimates, it may also be low for amosite.

Ingestion from Water

Asbestos is commonly found in domestic water supplies. Samples from 365 cities have been collected and analyzed by electron microscopy by the U.S. EPA. Of these, 45 percent had detectable levels of asbestos, usually of the chrysotile variety (Millette, 1979). Table 3 lists the distribution of the concentrations of these samples.

Earlier, asbestos had been reported in a variety of Canadian water supplies (Cunningham and Pontefract, 1971). These waters were found to contain from 2.0 to 172.7 x 10^6 fibers/l. (In this subsection fibers will denote all EM-countable fibers, irrespective of length). Two U.S. river systems were also reported to contain chrysotile at average levels of from 0.3 to 1.5 $\mu g/l$ (Nicholson and Pundsack, 1973). Other reports include that of Kay (1973) who found from 0.1 to 4 x 10^6 f/l in various Canadian drinking water sources.

TABLE 3

Distribution of Reported Asbestos Concentrations in Drinking Water from 365 Cities in 43 States, Puerto Rico, and the District of Columbia[a]

Asbestos Concentration (10^6 fibers/l)	Number of Cities	Percentage of Samples
Below detectable limits[b]	110	30.1
Not statistically significant	90	24.6
Less than 1	90	24.6
1-10	34	9.3
Greater than 10	41	11.2
Total	365	99.8

[a] Millette, 1979

[b] For these analyses average detectable limits were 5×10^5 fibers/l. However, significant variations occurred in some instances due to the presence of nonasbestos fibers.

During 1973, large amounts of asbestos-like fibers of amphibole minerals were found in the waters of Lake Superior, the source of drinking water for Duluth, Minnesota, and other cities (Cook, et al. 1974, 1976; Nicholson, 1974). Fiber concentrations during normal lake conditions ranged from 20×10^6 to 75×10^6 f/l and from about 5 to 30 μg/l in terms of mass (Nicholson, 1974). During storm conditions amphibole fiber concentrations as high as 600×10^6 f/l were observed (Cook, et al. 1976). Filtration plants now used in Duluth maintain fiber concentrations below 0.1×10^6 f/l (Millette, 1979).

Certain U.S. water systems currently have high levels of asbestos as a result of serpentine or amphibole deposits in their watersheds. These include Everett, Washington, with concentrations of chrysotile above 10^7 f/l; Seattle, with from 1 to 10×10^6 f/l; and San Francisco, with chrysotile concentrations about 10^7 f/l in some systems (Millette, 1979; Cooper, et al. 1978).

Under certain conditions, asbestos-cement (A/C) pipe may also contribute asbestos to municipal water supplies. Asbestos fiber concentrations in A/C pipe distribution systems were found to be as high as 38×10^6 chrysotile and 4×10^6 amphibole fibers/l in one Florida city; 17×10^6 in another Florida town; and 47×10^6 f/l in a Kentucky A/C pipe system. Water at the end of a little-used A/C pipe line in Massachusetts contained as much as 480×10^6 chrysotile f/l (Millette, 1976). Many of the A/C pipe systems in Connecticut have been sampled and analyzed (Craun, et al. 1977). The majority of samples taken after transit through A/C pipe showed concentrations under 1×10^6 f/l, and only one sample was over 10×10^6 f/l.

While there are an estimated 200,000 miles of A/C pipe now in use in the United States, it is apparent that not all A/C pipe sheds fibers. If the water is nonaggressive the pipe does not erode and contribute fibers to the water (Hallenbeck, et al. 1978).

A study (Buelow, et al. 1980) of 10 A/C pipe systems showed that fibers were added to the water by the A/C pipes of the 5 systems with aggressive water (Aggressiveness Index <10.0) and little effect was seen in the non-aggressive systems. In two systems the pipe was eroded to a depth of 0.3 cm, in one case in a period of only 5 years. In this system fiber counts as high as 550 x 10^6 f/l were measured in the distribution network versus 800,000 at the well source. In a third system high concentrations at a dead end sample were attributed to debris from tapping and drilling of pipes in the network.

Sampling of representative water utilities throughout the United States has indicated that over half of the samples had water which was moderately aggressive and 16.5 percent had very aggressive water (Table 4) (Millette, et al. 1979b). Water supplies in both the very aggressive and moderately aggressive categories are potentially capable of eroding asbestos-cement pipe (i.e., 68.5 percent of U.S. water systems) although the very aggressive waters could be expected to result in the contribution of much higher fiber concentrations.

Most data on asbestos in water are expressed in terms of fiber concentrations, enumerating fibers of all sizes using appropriate electron microscope techniques. Some estimates exist (Millette, 1979) relating chrysotile fiber concentrations to mass concentrations. Because the number-to-mass relationship is highly dependent on average fiber length and diameter, knowledge of the source of the fibers in the water is important in determining a conversion factor. Some average conversion factors are listed in Table 5.

TABLE 4

Representative Average Water Utility Aggressiveness Indices[a]

Highly aggressive[b]	16.5 percent
Moderately aggressive[c]	52.0 percent
Nonaggressive[d]	31.5 percent

[a] Millette, et al. 1979b

[b] Highly aggressive: $pH + \log_{10}(AH) < 10.0$

[c] Moderately aggressive: $pH + \log(AH) = 10.0 - 12.0$

[d] Nonaggressive: $pH + \log(AH) > 12.0$
where A = total alkalinity in mg/l, $CaCO_3$
H = calcium hardness as mg/l, $CaCO_3$

TABLE 5

Relationship of Total Fiber Counts by Electron Microscopy and Mass of Chrysotile Asbestos in Water*

Fiber Source	Average Mass in μg of 10^6 Fibers of All Lengths
Natural erosion of serpentine rock (shorter fibrils)	0.002
A/C pipe (longer fibers)	0.01
Contributions from commercial dump site runoff and untreated discharge (more fiber bundles)	0.05

*Source: Millette, 1979

Similar information on the relationship of fiber count and mass has been published by Kay (1973), whose data suggest that 10^6 fibers corresponds to from 2 x 10^{-4} to 2 x 10^{-3} µg in water systems. Data on asbestos concentrations from erosion of fibers from A/C cooling tower panels indicate that the mass of 10^6 fibers is from 0.01 to 0.2 µg (Lewis, 1977).

Based on the aforementioned data, it is concluded that the majority (approximately 95 percent) of water consumers in the United States are exposed to asbestos fiber concentrations of less than 10^6 f/l. In a few areas people are exposed to concentrations between 1 and 10 million f/l with intermittent exposures over 100 million f/l. There is at least one area where continuous exposure is over 100 million f/l. Persons using asbestos-cement pipe in areas where the water is nonaggressive or is treated to prevent corrosion are generally not additionally exposed. In areas of aggressive water, however, the consumer may be exposed to added asbestos fiber concentrations of from fewer than 1 million to over 100 million fibers per liter, depending on factors such as length of pipe, flow rate, and mineral content of the water.

The mass concentrations of chrysotile asbestos in the water of cities with less than 10^6 f/l are likely to be less than 0.01 µg/l, corresponding to a daily intake of less than 0.02 µg. However, in areas with significant contamination, whether from natural sources, man's activities, or erosion from A/C pipes, the intake of asbestos from water sources can exceed 2 µg/day.

Ingestion from Food

There are scant data on the contribution of food products to population asbestos exposure. Cunningham and Pontefract (1971) showed that various beers and wines could contain quantities of asbestos fibers similar to those found in water systems (10^6 to 10^7 f/l). The source of this contamination could be from natural water sources or from the erosion of asbestos fibers from filters used to purify the product. Asbestos filters are currently used for the purification of beverages and a variety of other food products, but little data exist on possible fiber contamination from such sources. Contamination of drinking water by fibrous glass and other synthetic fibers used in cartridge filters has been measured at concentrations in excess of 10^9 f/l (Cook, et al. 1978).

Exposure from Drugs

Erosion of chrysotile from asbestos filters, used to purify parenteral drugs, has been documented (Nicholson, et al. 1972). Contamination levels up to 1 µg/dose were noted in approximately one-third of drugs tested, indicating that filter erosion can be significant. Because of these findings, the use of asbestos filters for drug purification, without subsequent clean-up, has been prohibited by the Food and Drug Administration (41 FR 16933).

Inhalation

General Population Exposures: Asbestos of the chrysotile variety has been found to be a ubiquitous contaminant of ambient urban air. A study of 187 quarterly composite samples collected in 48 U.S. cities from 1969 to 1970 showed chrysotile asbestos to be present in virtually all metropolitan areas (Nicholson, 1971a; Nicholson and Pundsack, 1973). Table 6 lists the distribution of values obtained in that study. Each represents an average of from five to seven 24-hour samples and thus averages over possible peak concentrations which could occur periodically or randomly. A second set of ambient air analyses is also shown for comparison (U.S. EPA, 1974). These studies utilized different analytical techniques but the results agree well. In both studies, 98.5 percent of the 24-hour samples had chrysotile asbestos

TABLE 6

Distribution of 24-Hour Chrysotile Asbestos Concentrations in the Ambient Air of U.S. Cities*

	Electron Microscopic Analysis			
	Mount Sinai School of Medicine		Battelle Memorial Institute	
Asbestos Concentration (ng/m^3) less than	Number of samples	Percentage of samples	Number of samples	Percentage of samples
1.0	61	32.6	27	21.3
2.0	119	63.6	60	47.2
5.0	164	87.7	102	80.1
10.0	176	94.2	124	97.6
20.0	184	98.5	125	98.5
50.0	185	99.0	127	100.0
100.0	187	100.0	127	100.0

*Source: Nicholson, 1974; U.S. EPA, 1974 concentrations of less than 20 ng/m^3. Of the three samples greater than 20 ng/m^3 analyzed by the Mount Sinai School of Medicine, one was in a city having a major shipyard and another in a city that had four brake manufacturing facilities. Thus, these samples may include a contribution from a specific source in addition to that of the general ambient air.

Similar data with the same range of mass concentrations have recently been reported from France, providing evidence of the presence of chrysotile in the ambient air of Paris (Sebastien, et al. 1976).

In a study of the ambient air of New York City, in which samples were taken during daytime working hours, values higher than those mentioned above were obtained (Nicholson, et al. 1971). These were 6- to 8-hour samples collected between 8:00 A.M. and 5:00 P.M., and they reflect what could be intermittently higher concentrations from construction activities or automobile usage during those hours compared to nighttime periods for example. Table 7 records the chrysotile content of 22 samples collected in the 5 boroughs of New York. It should be noted that the samples analyzed in all of the studies discussed above were taken during a period when fireproofing highrise buildings by spraying asbestos-containing materials was permitted. The practice was especially common in New York City. While no sampling station was known to be located adjacent to an active construction site, unusually high levels could nevertheless have resulted from the procedure.

To determine if construction activities could indeed be a significant source of chrysotile fiber in the ambient air, 6- to 8-hour daytime sampling was conducted in lower Manhattan in 1969 near sites where extensive spraying of asbestos-containing fireproofing material was taking place. Table 8 shows the results of this sampling and demonstrates that spray fireproofing

TABLE 7

Chrysotile Content of Ambient Air in New York City by Borough

(6- to 8-Hour Daytime Samples)*

Sampling Locations	Number of Samples	Asbestos air level in 10^{-9} g/m^3 (ng/m^3)	
		Range	Average
Manhattan	7	8-65	30
Brooklyn	3	6-39	19
Bronx	4	2-25	12
Queens	4	3-18	9
Staten Island	4	5-14	8

*Source: Nicholson, et al. 1971

TABLE 8

Chrysotile Air Levels Near Spray Fireproofing Sites in New York City (6- to 8-Hour Daytime Samples)*

Sampling Locations (distance from site)	Number of Samples	Asbestos air level 10^{-9} g/m^3 (ng/m^3)	
		Range	Average
1/8 - 1/4 mile	11	9 - 375	60
1/4 - 1/2 mile	6	8 - 54	25
1/2 - 1 mile	5	3.5 - 36	18

The above concentrations reflect both downwind and upwind sampling locations.

*Source: Nicholson, et al. 1971

did contribute significantly to asbestos air pollution. In some instances, chrysotile asbestos levels approximately 100 times the concentrations typically found in ambient air were observed.

Asbestos contamination has also been documented by analysis of samples collected within buildings. In a study of 116 samples collected in or near 19 buildings (primarily office) in 5 U.S. cities, average chrysotile air concentrations ranged from 2.5 ng/m^3 to 200 ng/m^3, with individual measurements from 0 to 800 ng/m^3 (Nicholson, et al. 1975). For the outside air, the variation for the average concentration at a given site extended from 0 to 48 ng/m^3. Buildings in which a loose asbestos fireproofing material was applied to the structural steel surfaces had evidence of significant asbestos contamination. Also, schools in which similar material had been applied have been found to be seriously contaminated. Optical fiber counts exceeding 2 f/ml in a library and other areas of student use were observed during activities which disturbed loose asbestos (Sawyer, 1977; Nicholson, et al. 1978). Ambient air chrysotile concentrations in schools, in absence of any disturbance of the asbestos ranged up to 2,000 ng/m^3 (Nicholson, et al. 1978; Sebastien, et al. 1976). Finally, analysis of the air of asbestos workers' homes indicate that chrysotile concentrations as high as 5,000 ng/m^3 can be encountered (Nicholson, et al. 1978).

Figure 1 summarizes the ranges of chrysotile concentrations in the variety of environmental and occupational circumstances discussed above. The concentration ranges are only approximate and in most cases are limited because of the limited number of samples taken in given circumstances. Extension to higher and lower concentrations would be expected with the availability of more data.

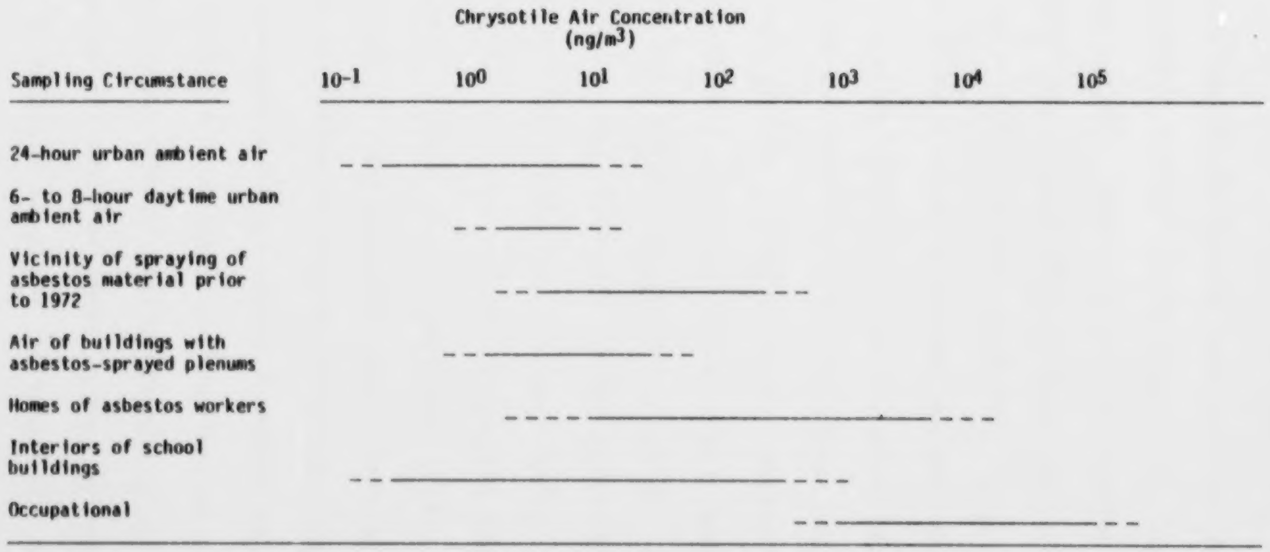


FIGURE 1

Environmental Air Concentrations of Chrysotile Asbestos

Source: Nicholson, et al. 1980a

Although the fate of the asbestos in inspired air is only approximately known, it appears that eventually more than half the asbestos inhaled will be swallowed (see Effects section). Assuming that an individual breathes 10 m^3 in 24 hours, most ambient air levels of chrysotile (1 to 10 ng/m^3) result in exposures to the gastrointestinal tract of from 0.01 to 0.05 μg/day of asbestos, although, in some circumstances, inhalation could produce gastrointestinal exposures exceeding 0.1 μg/day. These exposures are to be compared with those from water ingestion which lead to daily intakes of less than 0.02 μg (see Ingestion from Water section). Though the data of Tables 3 and 6 are not related to the same population bases, it would appear that inhalation can give rise to exposures at least equal to that of direct ingestion for most of the population of the United States.

Only after 1966 has occupational monitoring attempted to quantify asbestos exposures by fiber counting techniques. Since then, considerable data have accumulated on occupational exposure of workers to asbestos. A large compilation of such data is included in the 1972 Asbestos Criteria Document (NIOSH, 1972). Levels during the period from 1966 through 1971 were generally under 10f (f>5μm)/ml, although concentrations exceeding 100 f/ml were observed, particularly in two plants producing amosite insulation materials and in uncontrolled textile mills. Data on earlier exposures are lacking although some estimates have been made of insulation-workers' exposure (Nicholson, 1976) and factory environments (BOHS, 1968; Newhouse and Berry, 1979). Although average exposures of 10 to 40 f/l are likely to have prevailed, peak or localized exposures in excess of 100 f/l would have been encountered often by some individuals.

For purposes of estimating dose-response relationships, those data that are available for given work environments will be discussed in conjunction with the measured health effects.

PHARMACOKINETICS

Absorption and Distribution

Ingestion: A key question in the evaluation of cancer risk associated with the ingestion of asbestos in water is whether microscopic fibers under normal alimentary canal conditions can migrate through the gastrointestinal mucosa. Such movement of fibers could enable their residence in bowel wall or, following hematogenous or lymphatic transport, the peritoneum and other organ tissues. This has been well answered by the work of Carter and Taylor (1980) who demonstrated the presence of amphibole fibers, characteristic of those in Duluth, Minn. drinking water, in tissue samples of liver, jejunum, and lung of deceased Duluth residents. Among 96 tissue specimens of 32 Duluth residents amphibole fibers were found in 60, with concentrations ranging from 3×10^5 to 16×10^5 fibers of all sizes/gram of tissue. Amphibole fibers were found in only 2 of 61 tissue specimens of 21 control subjects deceased in Houston, Texas and St. Paul, Minn. As air sampling gave no evidence of amphibole air contamination in Duluth, the authors attribute the highly significant evidence ($p <0.001$) of tissue contamination to transmucosal uptake of fibers ingested by drinking amphibole contaminated Duluth water.

Some studies of tissues of animals that had ingested fibers report no evidence of fiber transport through the gastrointestinal lining (Gross, et al. 1974). These results, however, have been called into question on the basis of the insensitivity of the assay technique used (Cooper and Cooper, 1978). Evidence for such movement is reported in other studies (Cunningham and Pontefract, 1973). Cunningham, et al. (1977) observed chrysotile fibers in the blood and tissues of rats which previously were fed a diet of one percent chrysotile asbestos for six weeks. Westlake, et al. (1965) identified chrysotile fibers in the colon mucosa of rats fed chrysotile asbestos. Scanning electron micrographs have revealed large amosite asbestos fibers penetrating epithelial cells of rat jejunal mucosa tissue (Storeygard and Brown, 1977). Kidney cortex tissue of neonate baboon fed chrysotile for nine days was found to contain a statistically significant ($p = 0.005$) excess of chrysotile fibers compared to kidney cortex tissue from an unexposed neonate baboon (Patel-Mandlik and Hallenbeck, 1978). Cunningham and Pontefract (1974) observed passage of chrysotile fibers from the blood across the placenta to the fetus.

Ingestion of small particles other than asbestos has also resulted in the subsequent observation of particle accumulation in tissues of animals. Mice that drank water suspensions of 2 μm diameter latex spheres for two months were found to have the latex particles accumulated in macrophages in intestinal Peyer's patches (LeFevre, et al. 1978). Latex particles of 0.22 μm were reported to migrate from rat stomachs to lymphatics of the mucosa and also to liver and kidney tissues (Sanders and Ashworth, 1960). Much larger particles of silica, opal phytoliths from plants, are observed in digested mesenteric lymph node and kidney tissue from sheep which eat cereal chaff and grains (Nottle, 1977).

Evidence for the human intestinal uptake ("persorption") of particles as large as 75 μm is provided by the observation of starch granules in blood only minutes after ingestion (Volkheimer, 1974). Sleep, smoking, and caffeine are reported to increase the number of starch particles in the blood. Dyed cellulose particles are also identified in human blood and urine following ingestion of specially stained plant food (Schreiber 1974). The cellulose fibers are found in urine several weeks after ingestion. Langer (1974) found asbestos fibers in extrapulmonary organ tissues of asbestos workers, although fewer than in lung and pleura tissue, and more fibers in kidney than in liver, pancreas, adrenal, or spleen tissue.

Human urine sediment examined by transmission electron microscopy may contain amphibole fibers which originate from ingestion of drinking water contaminated with these mineral fibers (Cook and Olson, 1979). Ingestion of filtered water results in eventual disappearance of amphibole fibers from urine. These observations provide direct evidence for the passage of mineral fibers through the human gastrointestinal mucosa under normal alimentary canal conditions. Measured concentrations of amphibole fibers eliminated in urine represent approximately 1×10^{-3} of the number of fibers ingested with drinking water. To the extent that some fibers are permanently retained by the body or eliminated by other routes after passage across the gastrointestinal wall, the urine concentrations are an underestimate of ingested fiber absorption.

Inhalation: Inhalation of asbestos dust is accompanied by ingestion of many fibers cleared from the respiratory tract by mucociliary action. The occurrence of peritoneal mesothelioma, excess gastrointestinal tract cancers, and possibly cancers at other nonrespiratory tract sites could result from migration of fibers through the gastrointestinal mucosa. Additionally, fibers may reach organs in the peritoneal cavity by transdiaphragmatic migration or lymphatic-hematogenous transport. However, this would likely be a very small contribution compared to transmucosal migration following ingestion. The amount of inhaled asbestos which is eventually ingested is important for an assessment of cancer risk based on the excess gastrointestinal cancer observed for occupational exposures (see Effects section).

Whether inspired asbestos fibers will be deposited in the lung depends strongly upon their diameter. Timbrell (1965) has shown that a fiber, independent of its length, behaves aerodynamically like a particle having a diameter three times as great. Brain and Volberg (1974) have developed a model for aerosol deposition in the respiratory tract according to aerodynamic parameters. They indicate that about 50 percent of particles with a mass median diameter of less than 0.1 μm will be deposited on nonciliated pulmonary surfaces. This fraction falls slowly to 25 percent at 1 μm and to zero at above 10 μm. Deposition on nasal and pharyngeal surfaces becomes important at 1 μm and rises rapidly to be the dominant deposition site for particles 10 μm in diameter or greater. Thus, few fibers with a diameter as large as 2 μm are likely to penetrate into the alveolear spaces, although finer fibers, even as long as 200 μm, may do so.

Once inhaled, a large fraction of the inhaled dust is rapidly cleared from the respiratory tract by mucociliary action although some fibers will remain in the lung and be found there decades after exposure (Pooley,1973; Langer, 1974). Because of the ubiquitous exposure of individuals to asbestos, chrysotile fibers can be found in the lungs of most urban dwellers (Langer, et al. 1971; Gross, et al. 1973). Additionally, larger fibers trapped in the lungs may become coated and form asbestos bodies. These can be readily observed by optical microscopy in tissue sections and in lung smears (Thomson, et al. 1963; Langer, et al. 1973). The number of fibers or asbestos bodies found in given circumstances depends strongly upon the nature of the previous exposure of the individual.

The clearance of asbestos from the respiratory tract of rats has been studied directly in a series of experiments (Morgan, et al. 1975; Evans, et al. 1973). Samples were made radioactive by neutron irradiation, which enabled the mass of asbestos in various tissues to be determined. In a series of 30-minute exposures with different varieties of asbestos, the deposition and clearance in the respiratory tract were followed. At the conclusion of the inhalation, the distribution in various organ systems was determined. The results are shown in Table 9. As can be seen, rapid clearance from the upper respiratory tract occurs with up to two-thirds of the fibers being swallowed and found in the gastrointestinal tract. Long term respiratory tract clearance or drainage via the lymphatics leads to additional dissemination.

Other data on the deposition and retention of inhaled asbestos have been reported by Wagner, et al. (1974). Figure 2 shows the dust content of rat lungs following exposures to different asbestos varieties. As can be seen, the chrysotile content of the lung does not build up as significantly as that of the amphiboles for similar exposure circumstances. This is likely the result of some dissolution of chrysotile by body fluids.

Excretion

Most inhaled or directly ingested asbestos particles which pass through the gastrointestinal tract are excreted in feces (Cunningham, et al. 1976). As mentioned previously, some fibers are absorbed by the gastrointestinal tract and are eventually eliminated through the urinary tract (Cook and Olson, 1979).

EFFECTS

Acute, Subacute, and Chronic Toxicity

Acute effects are of little consequence in the inhalation exposure of individuals to high concentrations of asbestos dust. Some temporary breathing difficulty has been reported by workers in various circumstances, but such discomfort has not limited employment in the industry.

Short-term effects have been described in a recent study by Harliss, et al. (1978) who found airflow abnormalities in 17 of 23 individuals examined

TABLE 9

Distribution of Fiber at the Termination of Exposure
(% of Total Deposited)[a,b]

Fiber	Nasal Passages[b]	Esophagus	GI Tract	Lower Respiratory Tract
Chrysotile A	9 ± 3	2 ± 1	51 ± 9	38 ± 8
Chrysotile B	8 ± 2	2 ± 1	54 ± 5	36 ± 4
Amosite	6 ± 1	2 ± 1	57 ± 4	35 ± 5
Crocidolite	8 ± 3	2 ± 1	51 ± 9	39 ± 5
Anthophyllite	7 ± 2	2 ± 1	61 ± 8	30 ± 8
Fluoramphibole	3 ± 2	1 ± 1	67 ± 5	29 ± 4

[a] Morgan, et al. 1975

[b] Mean and SD

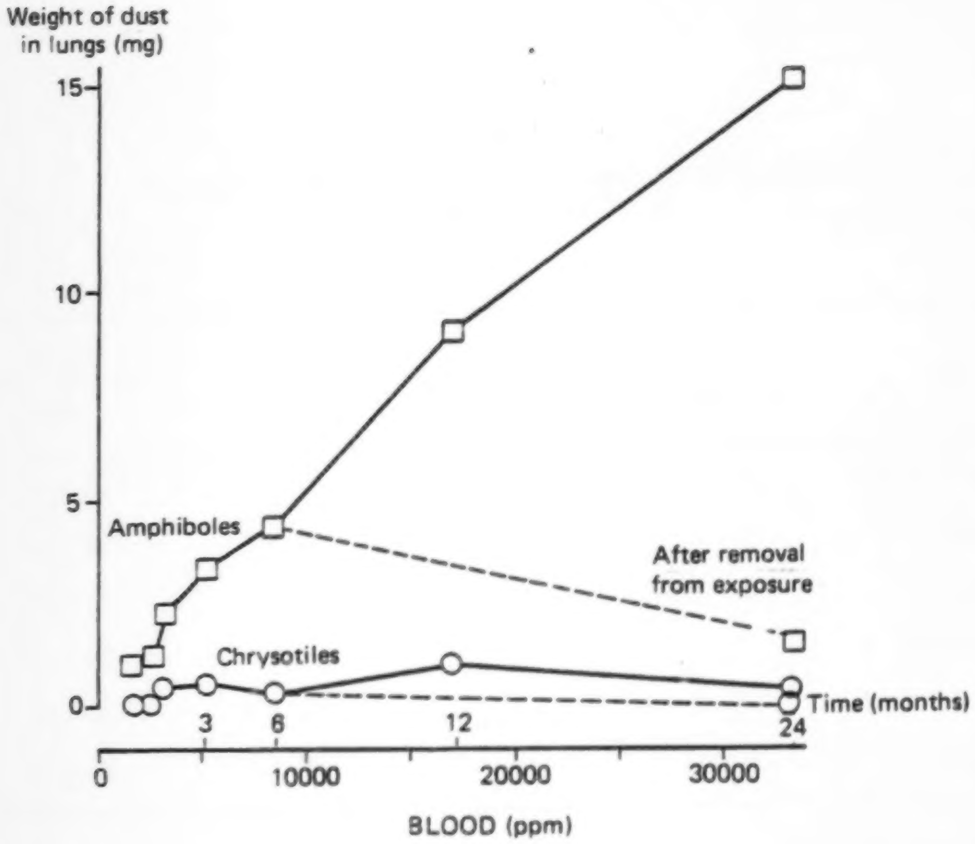


FIGURE 2

Mean Weight of Dust in Lungs of Rats in Relation to Dose and Time

Source: Wagner, et al. 1974

1.5 and 8.0 months following a relatively intense five-month exposure to asbestos. Of the 17, 12 were nonsmokers or current light or ex-light smokers (less than 10-pack years). The obstructive abnormalities were usually present in measurements both of one minute forced expiratory volume and of closing volume determinations.

Although human data on initial changes are unavailable, Holt, et al. (1964) described early (14-day) local inflamatory lesions found in the terminal bronchioles of rats following inhalation of asbestos fibers. These consisted of multinucleated giant cells, lymphocytes and fibroblasts. Progressive fibrosis followed within a few weeks of the first exposure to dust. (These early alterations in animals may be related to the early human findings above). Davis, et al. (1978) described similar early lesions in rats consisting of a proliferation of macrophages and cell debris in the terminal bronchioles and alveolae.

Jacobs, et al. (1978) fed rats 0.5 mg or 50 mg of chrysotile daily for 1 week or 14 months and subsequently examined gastrointestinal tract tissue by light and electron microscopy. No effects were noted in esophagus, stomach, or cecum tissue but structural changes in the ileum were seen, particularly of the villi. Considerable cellular debris was present by light microscopy in the ileum, colon, and rectum tissue. The electron microscopic data confirmed that of light microscopy and indicated the observed changes were consistent with a mineral-induced cytotoxicity.

A single oral administration of from 5 to 100 mg/kg of chrysotile to rats has produced a subsequent increase in thymidine in the stomach, duodenum, and jejunum (Amacher, et al. 1975). This suggests that an immediate response of cellular proliferation and DNA synthesis may be stimulated by chrysotile ingestion.

The long-term disease entity, asbestosis, resulting from the inhalation of asbestos fibers is a chronic, progressive pneumoconiosis. It is characterized by fibrosis of the lung parenchyma, usually radiologically evident after 10 years from first exposure, although changes can occur earlier following more severe exposures. Shortness of breath is the primary symptom; cough is less common; and signs such as rales, finger clubbing, and, in later stages of the disease, weight loss appear in a proportion of cases. The disease was first reported 7 decades ago (Murray, 1907) and has occurred frequently among workers occupationally exposed to the fiber in ensuing years. Characteristic X-ray changes are small, irregular opacities, usually in the lower and middle lung fields, often accompanied by evidence of pleural fibrosis or thickening, and/or pleural calcification. Both the visceral and, more commonly, parietal pleura may be involved. The mechanism of action and translocation of asbestos fibers to the parietal pleura is uncertain; both direct migration (Kiviluoto, 1960) or transport via lymphatics (Taskinen, et al. 1973) have been suggested.

Currently, 50 to 80 percent of individuals in occupational groups with exposures beginning more than 20 years earlier have been found to have abnormal X-rays. These include asbestos insulation workers (Selikoff, et al. 1965), miners and millers (Mount Sinai, 1976) and asbestos factory employees (Lewinsohn, 1972). In many circumstances the disease progresses following cessation of exposure; in a group employed in an asbestos factory for various periods of time between 1941 and 1954, X-ray changes were observed years following exposure in individuals having exposures as short as one week (Personal communication, I.J. Selikoff).

Restrictive pulmonary dysfunction is also seen with asbestos exposures and may be accompanied by diffusional defects or airway obstruction (Bader, et al. 1961). In the early stages of asbestosis, there is limited correlation between physiologic parameters, such as lung function tests. Later, X-ray changes and the lung function deficits are more highly correlated, but still incompletely so.

The above chronic effects are common among occupational groups directly exposed to asbestos fibers. They also, however, extend to those employed in other trades working near the application or removal of asbestos. Among workers other than insulators employed at a shipyard for longer than 15 years, 48 percent were found to have abnormal X-rays (Selikoff, et al. 1979b). Similar data were obtained in a study of maintenance personnel in a chemical plant (Lilis and Selikoff, 1979). Even family contacts (wives, children, etc.) of workers can be affected. Anderson, et al. (1976) have shown that 36 percent of 626 family contacts of workers employed some time between 1941 and 1954 at an asbestos insulation manufacturing facility had X-ray abnormalities years later characteristic of asbestos exposure.

In addition to disease and disablement during life, asbestosis has accounted for a large proportion of deaths among workers. The first reports of the disease (Auribault, 1906; Murray, 1907) described complete eradication of working groups. Much improvement in dust control has taken place in the industry since the turn of the century, but even recently those exposed in extremely dusty environments, such as textile mills, may have as much as 40 percent of their deaths attributable to this cause (Nicholson, 1976). Groups with lesser exposures for 20 or more years, such as in mining and milling (Mount Sinai, 1976) or insulation work (Selikoff, et al. 1979a) may have from 5 percent to 20 percent of their deaths from pneumoconiosis. All varieties of asbestos appear equally capable of producing asbestosis, in both man (Irwig, et al. 1979) and animals (Wagner, et al. 1974). In groups exposed at lower concentrations such as the families of workers, there is less incapacitation, and death from asbestosis has not been reported.

Extra-pulmonary chronic effects reported include "asbestos corns" from the penetration of asbestos fibers into the skin and their incorporation in dermal layers, and instances of Caplan's syndrome (rheumatoid pneumoconiosis). No chronic, nonmalignant gastrointestinal effects are reported.

Teratogenicity

No data exist on the presence or absence of teratogenic effects from the inhalation or ingestion of asbestos, although transplacental transfer of asbestos has been reported (Pontefract and Cunningham, 1973; Cunningham and Pontefract, 1974)

Mutagenicity

In a preliminary study chromosomal aberrations were seen in Chinese hamster cells cultured in a medium containing 0.01 mg/ml of either chrysotile or crocidolite (Sincock and Seabright, 1975). No chromosomal aberrations were seen in culture with coarse glass fibers or with control media. A more extensive series of experiments by Sincock (1977), using several chrysotile and crocidolite samples, showed that both positive transformation of morphology and positive genetic responses result from the passive inclusion of asbestos in culture media of CHO-K1 Chinese hamster cells. Very fine fibrous glass produced the same abnormalities, but chemically leached asbestos fibers produced fewer abnormalities than those untreated. The principal results are shown in Table 10.

Chamberlain and Tarmy (1977) tested UICC asbestos samples of chrysotile, amosite, anthophyllite, and samples of superfine chrysotile on several strains of *E. coli* and *S. typhimurium* bacterial systems in which mutagenicity to exogenous materials appears to correlate well with animal carcino-

TABLE 10

Effects of Different Treatments on Chromosomes of CHO-KI - Chinese Hamster Cells*

	SFA Chryso-tile	Rhodesian Chryso-tile a	Canadian Chryso-tile b	UICC Crocido-lite	UICC Antho-phyllite	UICC Amosite	Glass 110	Control
Polyploids	28	23	27	26	2	14	3	4
Cells with fragments	13	14	11	10	10	16	0	0
Other abnormalities	33	9	15	29	9	13	0	0
Percent abnormal karyotypes		62	34	39	56	26	41	3

	Rhodesian Chryso-tile a	Rhodesian Chryso-tile a Leached	Canadian Chryso-tile b	Canadian Chryso-tile b Leached	UICC Crocido-lite	UICC Crocido-lite Milled	Glass 110	Control
Polyploids	23	6	26	10	26	6	6	4
Cells with fragments	13	0	9	0	14	9	0	0
Other abnormalities	10	0	16	4	28	3	0	0
Percent abnormal cells	34	6	42	14	57	16	6	4

*This table summarizes the principal results reported in Sincock (1977). Results were obtained using 48-hour exposure; 100 cells were scored from each culture. Categories of genetic damage were not mutually exclusive.

genic test data. Several positive and negative controls were used in all experiments. No mutagenicity was observed in any of the bacterial strains. The authors point out that prokaryotic cells (bacteria) do not phagocytize the fibers as do eukaryotic cells, such as macrophages.

Carcinogenicity - Animal Data

Ingestion: Limited data exist on the carcinogenicity of asbestos administered by ingestion. With the exception of an abstract which reported negative data from 12 animals, published in 1967 (Bonser and Clayson, 1967), no reports were extant on the effects of ingested asbestos until the finding of large amounts of cummingtonite-grunerite fibers in Lake Superior and the drinking water of Duluth, Minn. focused attention on the problem. As an outgrowth of the Reserve Mining Company trial in which the federal government sought abatement of the Lake Superior pollution, two compilations from four laboratories were made of studies which showed negative results on the ingestion of asbestos.

Smith (1973) reported results of feeding 45 hamsters 1 percent chrysotile or amosite in their diet. A neoplasm of the mesentry of the colon was found, which was discounted because no fibers were identified in the tumor; no details were given concerning how the fibers were sought. The actual dosage of asbestos was not given, nor were other relevant experimental details provided. However, the finding of fibers in tumor tissue would be unlikely and, as these tumors are rare in hamsters, this result cannot be dismissed out of hand.

Gross, et al. (1974) reported the results of a series of feeding experiments with chrysotile and crocidolite. The data were the unpublished results of various experiments conducted over the previous 10 years by three laboratories. All available data on these experiments are listed in Table 11. The data are flawed for several reasons. The numbers in each experimental group were small, the doses administered limited, and significant information on experimental procedures lacking. Also, systematic histological examination, which was of most significance, was done on only 53 of over 200 animals.

Wagner, et al. (1977a) fed groups of 32 rats 100 milligrams per day of chrysotile or talc in malted milk for 100 days over a 6-month period of time. A small decrease in survival time was observed in the two study groups: 614 and 618 days versus 641 for the controls. Two gastric leiomyosarcomas were observed, one in each exposure group. Interpretation of the results of this experiment, too, is difficult because of the small number of animals in experimental groups.

As an outgrowth of concern for the use of asbestos filters in the purification of wine products and the possible effects of erosion of asbestos fibers from those filters into the final product, a study was undertaken in which asbestos filtered material was fed to rats (Gibel, et al. 1976). Twelve malignant tumors developed in experimental animals, including four kidney tumors. No tumors of this site were found in control groups. This observation of renal cancer takes on significance in light of the finding of an elevated risk of kidney cancer among asbestos insulation workers (Selikoff, et al. 1979a) and a high excretion of asbestos fiber in the urine of humans drinking fiber-contaminated water (Cook and Olson, 1979). However, this report provides only limited experimental detail, and the filter material was composed of sulfated cellulose and a condensation resin in addition to 52.6 percent chrysotile asbestos. The presence of other substances confounds the study in relation to asbestos carcinogenicity.

TABLE 11

Summary of Experiments on the Effects of Oral Ingestion of Asbestos

Animal Species	Material Administered	Dosage	Animals Examined for Tumors	Findings (malignant tumors)	Average Survival Time
		Gibel, et al. (1976)			
25 male and 25 female Wistar rats	asbestos filter material containing 52.6% chrysotile	50 mg/kg bw/day in the diet for life	42	4 kidney carcinomas 3 reticulosarcomas 4 liver-cell carcinomas 1 lung carcinoma	441 days
25 male and 25 female Wistar rats	talc	50 mg/kg bw/day in the diet for life	45	3 liver-cell carcinomas	649 days
25 male and 25 female Wistar rats	control	control	49	2 liver-cell carcinomas	702 days
		Wagner, et al. (1977a)			
32 Wistar SPF rats	UICC Canadian chrysotile in malted milk powder	100 mg/day 5 days/week for 100 days	32	1 gastric leiomyosarcoma	618 days
32 Wistar SPF rats	Italian talc	100 mg/day 5 days/week for 100 days	32	1 gastric leiomyosarcoma	614 days
16 Wistar SPF rats	control	control	16	none	641 days
		Gross, et al. (1974)			
10 male rats	ball-milled chrysotile mixed with laboratory chow	5% by weight of feed mix for 21 months	10	none	sacrificed

TABLE 11 (continued)

Summary of Experiments on the Effects of Oral Ingestion of Asbestos

Animal Species	Material Administered	Dosage	Animals Examined for Tumors	Findings (malignant tumors)	Average Survival Time
			Gross, et al. (1974)		
5 "laboratory" rats	control	control	5	none	sacrificed
31 Wistar SPF rats	Rhodesian chrysotile 0.2%-0.4%	10 mg weekly for 16 weeks	31 less "a few"	2 breast carcinomas	not stated
33 Wistar SPF rats	crocidolite in butter 0.2% - 0.4% mixture	5 mg weekly for 16 weeks	33 less "a few"	none	not stated
34 Wistar SPF rats	crocidolite in butter 0.2% - 0.4% mixture	10 mg weekly for 16 weeks	34 less "a few"	1 lymphoma	not stated
24 Wistar SPF rats	control (butter)	control	(24?)	3 breast carcinomas 1 thigh sarcoma	not stated
35 Wistar SPF rats	NW Cape crocidolite in butter (0.2%-0.4%)	10 mg weekly for 18 weeks	35 less "a few"	none	not stated
28 Wistar SPF rats	Transvaal crocidolite in butter (0.2% to 0.4%)	10 mg weekly for 18 weeks	28 less "a few"	none	not stated
24 Wistar SPF rats	control (butter)	control	(24?)	none	not stated

TABLE 11 (continued)

Summary of Experiments on the Effects of Oral Ingestion of Asbestos

Animal Species	Material Administered	Dosage	Animals Examined for Tumors	Findings (malignant tumors)	Average Survival Time
			Cunningham, et al. (1977)		
10 male Wistar rats	1% chrysotile+		7	2 kidney 1 peritoneal 1 lymphoma 1 fibrosarcoma 1 brain 1 pituitary	not given
10 male Wistar rats	control		8	1 peritoneal fibrosarcoma	not given
40 male Wistar rats	1% chrysotile	not given	36	3 thyroid 1 bone 1 liver 1 jugular body 2 leukemia/lymphoma 1 adrenal 1 large intestine anaplastic carcinoma 1 small intestine fibrosarcoma	not given
40 male Wistar rats	control		38	1 thyroid 1 liver 2 adrenals 1 kidney nephroblastoma 1 leukemia/lymphoma 5 subcutaneous tissue	not given

Cunningham, et al. (1977) conducted two limited feeding studies of male Wistar rats. One percent chrysotile asbestos with five percent corn oil was added to rat chow diet and fed to groups of 10 and 40 rats in two separate experiments. In the first study, six of seven surviving animals were found with tumors whereas only one malignancy was observed in eight controls (see Table 11). No gastrointestinal tumors were seen, but two of the treated group tumors were kidney nephroblastomas. In the second larger study, 11 tumors each were observed in treated and control groups of 40 animals. Two of the malignancies in the asbestos-fed group were of the gastrointestinal tract and one of the control group was a nephroblastoma, lessening the significance of the finding of this tumor in the other treated group. With the limited number of animals in this study, the evidence for carcinogenicity of asbestos (by feeding) is inconclusive.

Currently, a very large feeding experiment is being conducted under the auspices of the National Institute of Environmental Health Sciences (NIEHS). Results, however, are not anticipated until late 1980. Meanwhile, all previously reported experiments on ingested asbestos, whether positive or negative, have significant limitations. To extrapolate such data to man for use as a criteria for a standard would not be appropriate.

Inhalation: Although lung cancer was suggested as being causally related to human asbestos exposure in case reports in 1935 (Lynch and Smith, 1935; Gloyne, 1935), strongly indicated to be so in 1947 (Merewether, 1947), and unequivocally associated in a cohort study by Doll (1955), no positive animal data of consequence were forthcoming until 1967 when Gross, et al. (1967) showed that lung cancer could be produced by asbestos inhalation exposure. An early experiment of Nordmann and Sorge (1941) described two lung tumors in 10 of 100 mice surviving 240 days following exposure to high concentrations of chrysotile. This work, however, was called into question by Smith, et al. (1965) on the basis of the histology of the malignancies. Lynch, et al. (1957) exposed AC/F, hybrid mice to commercial chrysotile and observed a higher incidence of pulmonary adenomas in exposed animals, 45.7 percent (58/127), compared to controls, 36.0 percent (80/222). No malignant tumors were reported, and the increase of adenomas was not significant at the 0.05 level.

The first unequivocal data showing a relationship between asbestos inhalation and malignancy was that of Gross, et al. (1967) who observed carcinomas in rats exposed to a mean concentration of 86 mg/m^3 chrysotile for 30 hours/week from the age of six weeks. Of 72 rats surviving for 16 months or longer, 19 developed adenocarcinomas, 4 developed squamous cell carcinomas, and 1, a mesothelioma. No malignant tumors were found in 39 control animals. A search was made for primaries at other sites which could have metastasized. None were found. These and other data are summarized in Table 12.

Reeves, et al. (1971) found 2 squamous cell carcinomas in 31 rats sacrificed after 2 years following exposure to about 48 mg/m^3 of crocidolite. No malignant tumors were reported in rabbits, guinea pigs, hamsters, or in animals exposed to similar concentrations of chrysotile or amosite. No details of the pathological examinations were given.

In a later study (Reeves, et al. 1974), malignant tumors developed in 5 to 14 percent of the rats surviving 18 months. Lung cancer and mesothelioma were produced by exposures to amosite and chrysotile and lung cancer by crocidolite inhalation. Again, significant experimental details were lacking; information on survival times and times of sacrifice would have been useful. Available details of the exposures and results are given in Table 13. While

TABLE 12

Summary of Experiments on the Effects of Inhalation of Asbestos

Animal Species	Material Administered	Dosage	Animals Examined for Tumors	Findings (malignant tumors)	Average Survival Time
Gross, et al. (1967)					
132 male white rats	ball-and-hammer-milled Canadian chrysotile with/without 0.05 ml intratracheal 5 percent NaOH	42-146 mg/m³ (mean conc., 86 mg/m³) for 30 hrs/week	72	17 adenocarcinomas 4 squamous-cell sarcomas 7 fibrosarcomas 1 mesothelioma	not available
55 male white rats	controls with/without 5 percent NaOH	control	39	none	not available
Reeves, et al. (1971)					
206 rats 106 rabbits 139 guinea pigs	ball-milled chrysotile, amosite, and	48 ± 2 mg/m³ for 16 hrs/week up to 2 yrs	not available	2 squamous-cell carcinomas in 31 animals from crocidolite exposure	no information periodic sacrifices were made
214 hamsters	crocidolite				
Reeves, et al. (1974)					
219 rats	ball-and-	48 ± 2 mg/m³ for	120 rats	10 malignant tumors in rats	no information
216 gerbils	hammer-milled	16 hrs/week up	116 gerbils	2 in mice (See Table 13)	periodic sacrifices
100 mice 72 rabbits 108 guinea pigs	chrysotile, amosite, and crocidolite	to 2 yrs	10 mice 30 rabbits 43 guinea pigs		were made

TABLE 12 (continued)

Summary of Experiments on the Effects of Inhalation of Asbestos

Animal Species	Material Administered	Dosage	Animals Examined for Tumors	Findings (malignant tumors)	Average Survival Time
			Wagner, et al. (1974)		
13 groups of approx. 50 and 15 of about 25 Wistar SPF rats	amosite anthophyllite crocidolite Canadian chrysotile Rhodesian chrysotile (UICC samples)	10.1 to 14.7 mg/m^3 for 1 day to 24 months, 35 hrs/week	849	(See Tables 14 and 15) All asbestos varieties produced mesothelioma and lung cancer, some from exposure as short as 1 day	669 to 857 days versus 754 to 803 for controls. Survival times not significantly affected by exposure.
			Wagner, et al. (1977a)		
CO Wistar male and female rats	superfine chrysotile	10.8 mg/m^3 37.5 hrs/wk for 3, 6, or 12 months		1 adenocarcinoma of the lung in 24 animals exposed for 12 months	
CO Wistar male and female rats	nonfibrous cosmetic talc			none	
			Davis, et al. (1978)		
46 groups of approx. Han SPF rats and 20 Han SPF rats	UICC samples of amosite chrysotile crocidolite	2 mg/m^3 and 10 mg/m^3 35 hours/wk for 224 days	208	7 adenocarcinomas 3 squamous-cell sarcomas 1 pleural mesothelioma 1 peritoneal mesothelioma (See Table 16)	not available sacrificed at 29 months
20 Han SPf rats	control	control	20	none	

TABLE 13

Experimental Inhalation Carcinogenesis[a]

Fiber	Exposure		Rats		Mice	
	Mass[b] (mg/m³)	Fiber[b] (f/ml)	Animals Examined	Malignant Tumors	Animals Examined	Malignant Tumors
Chrysotile	47.9	54	43	1 lung papillary carcinoma 1 lung squamous-cell carcinoma 1 pleural mesothelioma	19	none
Amosite	48.6	864	46	2 pleural mesotheliomas	17	none
Crocidolite	50.2	1,105	46	3 squamous-cell carcinomas 1 adenocarcinoma 1 papillary carcinoma - all of the lung	18	2 papillary carcinomas of bronchus
Controls			5	none	6	1 papillary carcinoma of bronchus

[a] Reeves, et al. 1974

[b] The asbestos was comminuted by vigorous milling, after which 0.08% to 1.82% of the airborne mass was of fibrous morphology (3:1 aspect ratio) by light microscopy.

the relative carcinogenicity of the fiber types was similar, it was noted that the fibrogenic potential of chrysotile, which had been substantially reduced in length and possibly altered (Langer, et al. 1978) by milling, was much less than that of the amphiboles. These results were also discussed in a later paper by Reeves (1976).

In an extensive series of experiments, Wagner, et al. (1974) exposed groups of Wistar SPF rats to the five UICC asbestos samples at concentrations from 10 to 15 mg/m^3 for times ranging from 1 day to 24 months. For all exposure times there were 50 adenocarcinomas, 40 squamous-cell carcinomas, and 11 mesotheliomas produced. None appeared prior to 300 days from first exposure. Considerable experimental detail is provided in the paper. The significant data are presented in Tables 14 and 15. These tumors follow a reasonably good linear relationship for exposure times of three months or greater. The incidence in the 1-day exposure group, however, is considerably greater than expected. It was noted that exposure had a limited effect on length of life. Average survival times varied from 669 to 857 days for exposed animals versus 754 to 803 days for controls. The development of asbestosis was also documented. The incidence of lung cancer was found to be greater in animals surviving 600 days. There were 17 lung tumors, 6 in animals with no evidence of asbestosis and 11 in rats with minimal or slight asbestosis. Cancers at extrapulmonary sites were also listed. Seven malignancies of ovary and 8 of male genitourinary organs were observed in groups of approximately 350 rats. None were observed in groups of 60 male and female controls. Incidence of malignancy at other sites was little different from that of controls. If controls are included from other experiments in which ovarian and genitourinary tumors were present, the comparative inci-

TABLE 14

Number of Rats with Lung Tumors or Mesotheliomas After Exposure to Various Forms of Asbestos Through Inhalation*

Form of Asbestos	No. of Animals	Adenocarcinomas	Squamous-cell Carcinomas	Mesothelioma
Amosite	146	5	6	1
Anthophyllite	145	8	8	2
Crocidolite	141	7	9	4
Chrysotile (Canadian)	137	11	6	4
Chrysotile (Rhodesian)	144	19	11	0
None	126	0	0	0

*Source: Wagner, et al. 1974

TABLE 15

Numbers of Rats with Lung Tumors or Mesotheliomas After Various Lengths of Exposure to Various Forms of Asbestos Through Inhalation[a]

Length of Exposure	No. of Animals	No. with Lung Carcinomas	No. with Pleural Mesotheliomas	% of Animals with Tumors
None	126	0	0	0.0
1 day	219	3[b]	2[c]	2.3
3 months	180	8	1	5.0
6 months	90	7	0	7.8
12 months	129	35	6	31.8
24 months	95	37	2	41.0

[a] Wagner, et al. 1974

[b] 2 exposed to chrysotile and 1 to crocidolite

[c] 1 exposed to amosite and one to crocidolite

dence in the exposure groups here lacks significance. No data were provided, however, on the variation of tumor incidence at extrapulmonary sites with asbestos dosage.

Wagner, et al. (1977a) also compared effects of inhalation of a superfine chrysotile to a pure, nonfibrous talc. One adenocarcinoma was found in 24 rats exposed to 10.8 mg/m^3 of chrysotile for 37.5 hours/week for 12 months.

Finally, in a study similar to Wagner's, Davis, et al. (1978) exposed rats to 2.0 or 10.0 mg/m^3 of chrysotile, crocidolite, and amosite (equivalent to from 430 to 1950 f/ml). Adeno- and squamous cell carcinomas were observed in chrysotile exposures, but not with crocidolite or amosite (see Table 16). One pleural mesothelioma was observed with crocidolite exposure, and extrapulmonary neoplasms included a peritoneal mesothelioma. A relatively large number of peritoneal connective tissue malignancies were also observed, including a leiomyofibroma on the wall of the small intestine. The significance of these tumors is speculative, however.

As discussed in the Pharmacokinetics section, inhalation exposures result in concomitant gastrointestinal exposures from the asbestos that is swallowed after clearance from the bronchial tree. While all inhalation experiments focused on thoracic tumors, those of Wagner, et al. (1974), Davis, et al. (1978) and, to a limited extent, Gross, et al. (1967) also included a search for tumors at extrathoracic sites. A limited number of these were found, but no association can be made with asbestos exposure.

One aspect of the inhalation experiments that is noteworthy is the significant number of pulmonary neoplasms that can be produced in the rat by inhalation as compared to other species (Reeves, et al. 1971, 1974). This points to the variability of species response to asbestos and the need for

TABLE 16

Experimental Inhalation Carcinogenesis in Rats*

	Exposure			
	Mass (mg/m^3)	Fiber (f>5μ/ml)	Number of Animals Examined	Malignant Tumors
Chrysotile	10	1,950	40	6 adenocarcinomas 2 squamous-cell carcinomas
Chrysotile	2	390	42	1 squamous-cell carcinoma 1 peritoneal mesothelioma
Amosite	10	550	43	none
Crocidolite	10	860	40	none
Crocidolite	5	430	43	1 pleural mesothelioma
Control			20	none

*Source: Davis, et al. 1978

an appropriate model before extrapolations to man can be made with confidence. The absence of significant gastrointestinal malignancy from asbestos exposure in animals, in contrast to that found in humans, may be the result of the use of inappropriate animal models.

Intrapleural Administration: Evidence that intrapleural administration of asbestos would result in mesothelioma was forthcoming in 1970 when Donna (1970) produced mesotheliomas in Sprague-Dawley rats treated with a single dose of 67 mg of chrysotile, amosite, or crocidolite. Reeves, et al. (1971) produced mesothelial tumors in rats (1 of 3 with crocidolite and 2 of 12 with chrysotile) by intrapleural injection of 10 mg of asbestos. Two of 13 rabbits injected with 16 mg of crocidolite developed mesotheliomas.

Stanton and Wrench (1972), in a series of experiments, demonstrated that major commercial varieties of asbestos, as well as various other fibers, produced mesotheliomas in as many as 75 percent of animals into which material had been surgically implanted. Extension of these experiments were reported in 1973 (Stanton, 1973). These results are summarized in Table 17. The authors concluded that the carcinogenicity of asbestos and other fibers is strongly related to their physical size, those fibers of a diameter less than 3 µm being carcinogenic and those of a larger diameter not carcinogenic. Further, samples treated by grinding in a ball mill to produce shorter length fibers were less likely to produce tumors. While the authors attributed the reduced carcinogenicity to a shorter fiber length, the question has been raised as to the effect of the destruction of crystallinity and perhaps other changes in the fibers occasioned by the extensive ball milling (Langer, et al. 1978).

Another comprehensive set of experiments was conducted by Wagner (Wagner, et al. 1973, 1977b). He, too, has produced mesothelioma from intra-

TABLE 17

Dose-response Data Concerning the Effects of Intrapleural Implantation of Asbestos and Other Fibers in Rats*

	Dose (mg)	No. of Rats with Mesotheliomas	Total no. of rats	% of Rats with Tumors
UICC-SRAS	1	2	25	8
Crocidolite	2	5	23	22
	10	11	27	41
	20	12	25	48
	40	14	23	61
Hand-cobbed	1	4	30	13
Virgin	20	10	24	42
Crocidolite	40	18	27	67
Special South African crocidolite	40	15	20	75
Partially pulverized crocidolite	40	8	25	32
UICC-SRAS amosite	40	15	25	60
UICC-SRAS chrysotile	40	15	26	58
Coarse fibrous glass	40	1	24	4
Glass wool	40	1	25	4
Fine AAA fibrous glass 3μm diameter				
uncoated	40	3	26	12
coated	40	5	28	18

*Source: Stanton and Wrench, 1972

pleural administration of asbestos to CD Wistar rats and demonstrated a strong dose-response relationship. Tables 18 and 19 list the results of these experiments.

Pylev and Shabad (1973) and Shabad, et al. (1974) reported mesotheliomas in 18 of 48 and in 31 of 67 rats injected with three doses of 20 mg of Russian chrysotile. Other experiments by Smith and Hubert (1974) have produced mesotheliomas in hamsters injected with 10 to 25 mg of chrysotile, 10 mg of amosite or anthophyllite, and 1 to 10 mg of crocidolite.

Various suggestions have been made that natural oils and waxes contaminating asbestos fibers might be related to their carcinogenicity (Harington, 1962; Harington and Roe, 1965; Commins and Gibbs, 1969). This, however, was not borne out in the experiments described above by Wagner, et al. (1973) or Stanton and Wrench (1972).

Intratracheal Injection: Intratracheal injection has been used to study the combined effect of administration of chrysotile with benzo(a)pyrene in rats or hamsters (see Synergism and/or Antagonism). In rats given three doses of 2 mg chrysotile (Shabad, et al. 1974) or hamsters given 12 mg of chrysotile (Smith, et al. 1970) no lung tumors were observed. However, the coadministration of benzo(a)pyrene did result in lung tumors.

Intraperitoneal Administration: Intraperitoneal injections of 20 mg of crocidolite or chrysotile produced three peritoneal mesotheliomas in 13 Charles River CD rats. Twenty mg of amosite produced no tumors in a group of 11 (Maltoni and Annoscia, 1974). They also injected 25 mg of crocidolite into 50 male and 50 female 17-week-old Sprague-Dawley rats and observed 31 mesothelial tumors in males and 34 in females.

In an extensive series of experiments, Pott and Friedrichs (1972) and Pott, et al. (1976) produced peritoneal mesotheliomas in mice and rats in-

TABLE 18

Percentage of Rats Developing Mesotheliomas After Intrapleural Administration of Various Materials[a]

Material	Percent of Rats with Mesotheliomas
SFA chrysotile (superfine Canadian sample)	66
UICC crocidolite	61
UICC amosite	36
UICC anthophyllite	34
UICC chrysotile (Canadian)	30
UICC chrysotile (Rhodesian)	19
Fine glass fiber (code 100), median diameter, 0.12 μm	12
Ceramic fiber, diameter, 0.5-1 μm[b]	10
Glass powder	3
Coarse glass fiber (code 110), median diameter, 1.8 μm	0

[a] Wagner, et al. 1977b

[b] Wagner, et al. 1973

TABLE 19

Dose-Response Data Following Intrapleural Administration of Asbestos to Rats*

Material	Dose (mg)	No. of Rats with Mesothelioma	Total no. of Rats	% of Rats with Tumors
SFA chrysotile	0.5	1	12	8
	1	3	11	27
	2	5	12	42
	4	4	12	33
	8	8	12	62
Crocidolite	0.5	1	11	9
	1	0	12	0
	2	3	12	25
	4	2	13	15
	8	5	11	45

*Source: Wagner, et al. 1973

jected with various commercial varieties of asbestos and other fibrous material. These results are shown in Table 20. Using experiments with intrapleural administration, the malignant response was altered by ball-milling fibers for 4 hours. The rate of tumor production was reduced from 55 percent to 32 percent and the time from onset of exposure to first tumor was lengthened from 323 to 400 days following administration of four doses of 25 mg of UICC Rhodesian chrysotile. In the case of the ball-milled fiber, 99 percent were reported to be smaller than 3 μm, 93 percent less than 1 μm, and 60 percent less than 0.3 μm.

A strong conclusion which can be drawn from the above experimental data is that large-diameter fibers (greater than 3 μm) are significantly less carcinogenic than finer fibers. The origin of the reduced carcinogenicity of shorter, ball-milled fibers is less clear as the relative contributions of shorter fiber length and the significant alteration of the crystal structure by input of physical energy are not, as yet, defined. Further, the extrapolation of data developed on size-dependent effects, from intrapleural or intraperitoneal administration to inhalation (where movement of the fibers in airways and subsequently through body tissues is strongly size-dependent) presents significant difficulties. Finally, since the number of smaller fibers in an exposure circumstance may be 100 times greater than those longer than 5 μm, the reduction of their carcinogenicity must be demonstrated at a level 100 times less before their contribution can be neglected.

Carcinogenicity - Human Data

The modern history of asbestos disease dates from the turn of the century, when two reports were published documenting uncontrolled conditions in asbestos textile factories. One, the testimony of H. Montague Murray (1907)

TABLE 20

Tumors in Abdomen and/or Thorax After Intraperitoneal Injection of Glass Fibers, Crocidolite, or Corundum in Rats[a]

Dust	Form[b]	I.P. Dose	Effective Number of Dissected Rats	No. of Days Before First Tumor	Average Survival Time of Rats with Tumors (days after injection)	Rats with Tumors (percent)	Tumor Type[c]					
							1	2	3	4	5	6
Glass fibers MN 104	f	2	73	421	703	27.4	17	3	-	-	1	1
Glass fibers MN 104	f	10	77	210	632	53.2	36	4	-	1	3	-
Glass fibers MN 104	f	2 x 25	77	194	367	71.4	47	6	2	-	-	-
Crocidolite	f	2	39	452	761	38.5	12	3	-	-	2	1
Corundum	g	2 x 25	37	545	799	8.1	1	-	-	2	2	2
UICC Rhodesian chrysotile	f	2	37	431	651	16.2	4	2	-	-	1	-
UICC Rhodesian chrysotile	f	6.25	35	343	501	77.1	24	3	-	-	-	-
UICC Rhodesian chrysotile	f	25	31	276	419	80.6	21	2	1	1	-	-
UICC Rhodesian chrysotile	f	4 x 25	33	323	361	54.5	16	2	-	-	-	-
UICC Rhodesian chrysotile	f	3 x 25 s.c.	33	449	449	3.0	-	-	1 s.c.	-	-	-
UICC Rhodesian milled	f	4 x 25	37	400	509	32.4	9	3	-	-	-	-
Palygorscite	f	3 x 25	34	257	348	76.5	24	2	-	-	-	-

TABLE 20 (continued)

Tumors in Abdomen and/or Thorax After Intraperitoneal Injection of Glass Fibers, Crocidolite, or Corundum in Rats[a]

Dust	Form[b]	I.P. Dose	Effective Number of Dissected Rats	No. of Days Before First Tumor	Average Survival Time of Rats with Tumors (days after injection)	Rats with Tumors (percent)	Tumor Type[c]					
							1	2	3	4	5	6
Glass fibers s + s 106	f	2	34	692	692	2.9	1	-	-	-	-	-
Glass fibers S + S 106	f	10	36	350	530	11.1	2	2	-	-	1	-
Glass fibers S + S 106	f	4 x 25	32	197	325	71.9	20	3	-	-	-	-
Gypsum	f	4 x 25	35	579	583	5.7	-	-	1	1	1	-
Henalite	f	4 x 25	34	249	315	73.5	17	8	-	-	-	-
Actinolite	g	4 x 25	39	-	-	-	-	-	-	-	-	-
Biotite	g	4 x 25	37	-	-	-	-	-	-	-	-	-
Haematite (precipit.)	g	4 x 25	34	-	-	-	-	-	-	-	-	-
Haematite (mineral)	g	4 x 25	38	-	-	-	-	-	-	-	-	-
Pectolite	g	4 x 25	40	569	569	2.5	-	-	-	1	1	1
Sanidine	g	4 x 25	39	579	579	2.6	-	1	-	-	-	-
Talc	g	4 x 25	36	587	587	2.8	1	-	-	-	-	-
NaCl (control)	-	4 x 2ml	72	-	-	-	-	-	-	-	-	-

[a] Source: Pott and Friedrichs, 1972; Pott, et al. 1976

[b] f = fibrous; g = granular

[c] Tumor Types are: 1 Mesothelioma; 2 Spindle cell sarcoma; 3 Polym-cell sarcoma; 4 Carcinoma; 5 Reticulum cell sarcoma; 6 Benign -- not evaluated in tumor rates

at a hearing concerning compensation, described severe pulmonary fibrosis found at autopsy in 1900 in the last survivor of a group of 10 workers first employed 14 years previously in a carding room. The second was the description by Auribault (1906) of deaths during the early years of operation of an asbestos weaving mill established at Conde-sur-Noireau, France, in 1890. During this period 50 men died, including 16 of 17 recruited from a cotton textile mill previously owned by the factory director.

With time, however, the spectrum of diseases associated with asbestos exposure continued to expand. In 1935 two clinical reports were published on lung cancer in asbestos workers who had died with evidence of pulmonary fibrosis (Lynch and Smith, 1935; Gloyne, 1935). While such reports were not sufficient to causally relate asbestos exposure to the lung cancer, the possibility was raised. In 1947 it was confirmed by substantial data which showed that 13 percent of a group of individuals who died with asbestosis in Great Britain also had bronchogenic carcinoma (Merewether, 1947). Mesothelioma, a rare tumor of the lining of the abdomen or chest, was first described in an asbestos worker in 1953 (Weiss, 1953) subsequently found to be frequently associated with potential asbestos exposure (Wagner, et al. 1960), and unequivocally related to such exposure in 1965 (Newhouse and Thomson, 1965). Gastrointestinal cancer also was found to be in excess among asbestos insulation workers in the United States (Selikoff, et al. 1964).

Currently, all major commercial asbestos varieties, chrysotile, amosite, and crocidolite, have been found to produce a significant incidence of asbestos-related disease among workers occupationally exposed in mining and milling, in manufacturing, and in the use of materials containing the fiber. The predominant route of exposure has been inhalation, although some asbestos may be swallowed directly or after being brought up from the respiratory tract. Not only has asbestos disease been found among individuals exposed to the fiber directly as a result of excessive work exposures in decades past, but asbestos-associated cancer has also been identified, albeit less frequently, among those with inhalation exposures of lesser intensity, including those who had worked near the application or removal of asbestos material, those with history of residing in the vicinity of asbestos plants, and those who had lived in the household of an asbestos worker.

Water Ingestion: Five studies have considered the relation of asbestos ingested in drinking water to gastrointestinal cancer. As an outgrowth of the contamination of Lake Superior by fibrous material in the tailings of an iron ore processing plant, the mortality of the population of Duluth was compared with that of Minnesota and Hennapin County (Minneapolis) for quinquenia to 1969 (Mason, et al. 1974). The relative death rates for digestive cancer, lung cancer, and all neoplasm were elevated from 16 to 49 percent. However, with the exception of colon/rectal cancer, which was highly elevated, no trends with time or consistency between male and female were clearly discernable. Because of this, Mason, et al. (1974) concluded that additional followup was necessary to determine if a hazard exists. Levy, et al. (1976) conducted a similar study with equivalent results. However, the short follow-up from the earliest possible exposure (1956) would make it unlikely that any positive result would be found. Furthermore, while the Reserve plant began production in 1956, current discharge levels did not begin until 1967 when a major plant expansion took place.

A study by Harrington, et al. (1978) reviewed malignancy in the Connecticut Tumor Registry from 1935 to 1973 to see if a correlation existed between the use of asbestos cement (A/C) pipe for public water supply and the incidence of gastrointestinal cancer. No association was found between the age-adjusted, sex-specific incidence data for stomach, colon, and rectal cancer and the use of A/C pipe. While some water supplies reported A/C pipe that was 45 years old in 1975, the majority (66 percent) of the population studied received water through A/C pipes that were only 25 years old. While the majority (56 percent) of A/C pipe systems in Connecticut have water which is considered aggressive under the AWWA Standard for A/C transmission and pressure pipe, fiber counts done on over 100 A/C pipe systems in Connecticut showed 98 percent to be under 10^6 f/l (J. Millette, personal communication).

A report published for the University of California analyzed the 1969-1971 cancer incidence from 721 census tracts of the five Bay Area Counties along with the chrysotile asbestos fiber concentrations in the drinking water (Cooper, et al. 1978). For the census tracts the chrysotile asbestos fiber counts ranged from below detectable limits to 36×10^6 fibers per liter.

The University of California investigators grouped the census tracts on a gradient of low-to-high asbestos counts and found significant dose-response gradients for the incidence of several cancers. Statistically significant positive trends were noted for white male lung and stomach cancer and white female gall bladder, esophageal, and peritoneal cancer. The census tracts were cross-classified using both asbestos count and tract socioeconomic status indicators of medium family income and medium school years completed. The positive dose-response effect between cancer incidence of certain sites and asbestos counts appeared to be independent of the effect of socio-economic status. The fact that the significant results are not restricted to one body site is not surprising considering the knowledge that asbestos fibers are probably transported throughout the body. For example, one study using rats has found that ingested fibers are deposited in the lung. (Cunningham, et al. 1977). An extension of this study (Cooper, et al. 1979) using six years of data showed a statistically significant association between asbestos levels in the San Francisco Bay area drinking water and cancers of the digestive tract.

A study by Wigle (1977) compared the cancer mortality in two areas of Canada with probable high concentrations of asbestos in drinking water with an area presumably having low concentrations. Only one published asbestos concentration is provided. Five values are listed from a personal communication with no details given on the sampling and analytical methods utilized. No data are provided to substantiate the assumed exposures of all of the "probably low exposure" group and five of the seven "possible high exposure" municipalities. The mortality experience was compared with that expected from Quebec rates, although for some sites it is known that the rural counties have lower cancer rates than Quebec, the rates of which are dominated by the urban center, Montreal. For example, the lung cancer rate of the rural counties near the asbestos mines is only two-thirds that of Quebec (McDonald, et al. 1971). Elevated rates for cancer of the stomach, colon, and rectum were seen among "high exposure" males (46 observed vs. 38.4 expected), "possible high exposure" females (103 vs. 91.3) and "probably low exposure" females (311 vs. 270.3). The rates for the other two male and one female groups were about 5 percent less than expected. In addition to the absense of sampling data on exposure, the small number of deaths observed seriously limits the study. For example, this document estimates that a 10^{-5} risk of death from asbestos ingestion may occur from exposures to 400,000 f/l. If there were no population migration into or from the highly exposed areas and everyone deceased in those municipalities were exposed for a lifetime to the concentrations indicated, the above criteria level would predict about ten excess deaths among the approximately 1,000 that occurred over the observation time of this study.

Insulation Application and Removal: A large study by Selikoff, et al. (1979a) best demonstrates the full spectrum of disease from asbestos exposure. They studied the mortality experience of 17,800 asbestos insulation workers from January 1, 1967 through December 31, 1976. These workers were exposed primarily to chrysotile prior to 1940, and to a mixture of chrysotile and amosite subsequently. No crocidolite is known to have been used in U.S. insulation material (Selikoff, et al. 1970). In this group, 2,271 deaths have occurred, and their analysis provides important insights into the nature of asbestos disease. Table 21 lists the expected and observed deaths by cause, and includes data on tumors less frequently found. Lung tumors are common and account for about 20 percent of the deaths; 8 percent are from mesothelioma of the pleura or peritoneum. Additionally, though, cancer of the gastrointestinal tract is significantly elevated; so, too, are cancer of the larynx, pharynx, and buccal cavity, and renal tumors. Other tumors are also increased, but not to a statistically significant degree for an individual site. Comparing the deaths from cancer and asbestosis in this group with those expected in the general population, more than 40 percent of the deaths among insulators can be attributed to their occupational exposure to asbestos fiber.

Table 21 lists the observed deaths as categorized on death certificates and as determined after a review of all autopsy and medical records (BE). The use of deaths characterized by the best available medical evidence for risk analysis is appropriate when one considers diseases that are virtually

TABLE 21

Deaths Among 17,800 Asbestos Insulation Workers in the United States and Canada January 1, 1967 - January 1, 1977[a,b]

Number of Men: 17,800
Man-Years of Observation: 166,853

Underlying Cause of Death	Expected	Observed		Ratio o/e	
		(BE)	(DC)	(BE)	(DC)
Total deaths, all causes	1,658.9	2,271	2,271	1.37	1.37
Total cancer, all sites	319.7	995	922	3.11	2.88
Cancer of lung	105.6	486	429	4.60	4.06
Pleural mesothelioma	c	63	25	--	--
Peritoneal mesothelioma	c	112	24	--	--
Mesothelioma, n.o.s.	c	0	55	--	--
Cancer of esophagus	7.1	18	18	2.53	2.53
Cancer of stomach	14.2	22	18	1.54	1.26
Cancer of colon-rectum	38.1	59	58	1.55	1.52
Cancer of larynx	4.7	11	9	2.34	1.91
Cancer of pharynx, buccal	10.1	21	16	2.08	1.59
Cancer of kidney	8.1	19	18	2.36	2.23
Deaths of less common malignant neoplasms					
Pancreas	17.5	23	49	1.32	2.81
Liver, biliary passages	7.2	5	19	0.70	2.65
Bladder	9.1	9	7	0.99	0.77
Testes	1.9	2	1	--	--
Prostate	20.4	30	28	1.47	1.37
Leukemia	13.1	15	15	1.15	1.15
Lymphoma	20.1	19	16	0.95	0.80
Skin	6.6	12	8	1.82	1.22
Brain	10.4	14	17	1.35	1.63
All other cancer	25.5	55	92	2.16	3.61
Noninfectious pulmonary diseases total	59.0	212	188	3.59	3.19
Asbestosis	c	168	78	--	--
All other causes	1,280.2	1,064	1,161	0.83	0.91

[a] Selikoff, et al. 1979a

[b] Expected deaths are based upon white male age specific mortality data of the U.S. National Center for Health Statistics for 1967-1975 and extrapolation to 1976.

[c] Rates are not available, but these have been rare causes of death in the general population.

BE: Best evidence. Number of deaths categorized after review of best available information (autopsy, surgical, clinical)

DC: Number of deaths as recorded from death certificate information only.

absent in the general population (asbestosis and mesothelioma). Since mesothelioma is not a common cause of death in other than asbestos-exposed individuals, its misdiagnosis on the death certificates of general population has little significance. However, as it is a major cause of death of asbestos-exposed workers, its proper diagnosis is necessary in order to evaluate the extent of occupational disease. Moreover, were it not to be properly characterized one would conclude that cancers of the liver and pancreas were elevated from asbestos exposure. Thus, one would have to consider excesses at these sites (as misdiagnosed on death certificates) rather than mesothelioma in evaluating abdominal cancers. Otherwise, the use of best evidence rather than death certificate information is a minor factor in the evaluation of gastrointestinal cancer. For example, among cancers of the esophagus, stomach, colon, and rectum in 2,271 consecutive deaths in insulation workers, 112 were listed at these sites on death certificates. Best evidence indicated that 118 occurred. This difference would have little effect upon the calculation of gastrointestinal cancer. On the other hand, peritoneal mesothelioma per se was specified in only 24 deaths where best evidence indicated 112 occurred from this disease. The difference was largely made up from overdiagnosed cancer of the pancreas (26 cases), cancer of the liver (14 cases), and from 55 mesotheliomas unspecified as to site.

The large number of deaths allows an analysis to be made of the onset of effects as related to time from first exposure. Figure 3 depicts the excess asbestos-related lung cancers and mesotheliomas according to time from onset of exposure. It is seen that an important rise in bronchogenic carcinoma occurs only after 25 years and mesothelioma and asbestosis after 30 years. This long-lapsed period is seen in individuals exposed continuously to relatively high concentrations of asbestos. At lower exposures, longer periods

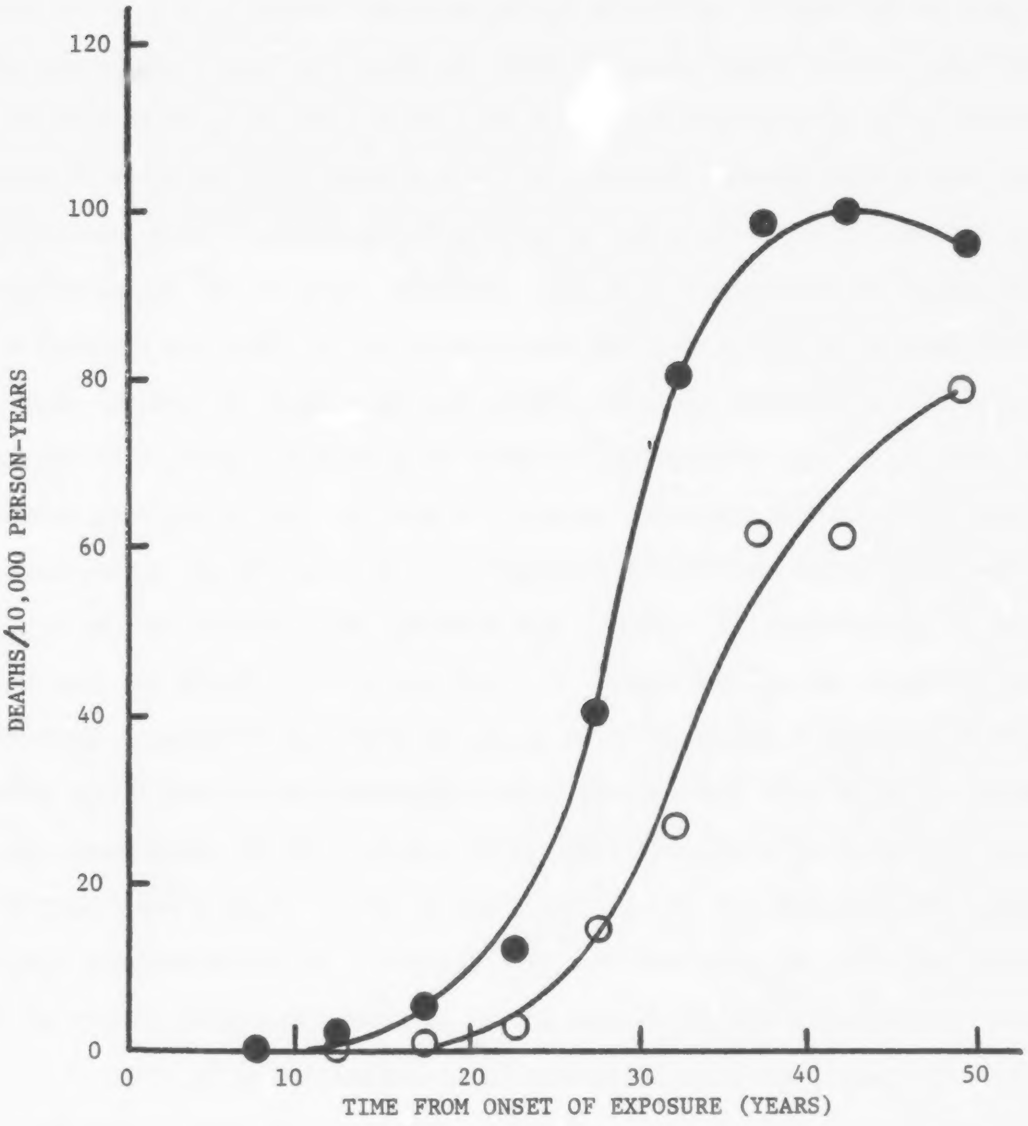


FIGURE 3

The Excess, Asbestos-related Mortality Rates for Lung Cancer and Mesothelioma According to Time from Onset of Asbestos Disease

Source: Selikoff, et al. 1979a
○= mesothelioma
●= lung cancer

from exposure onset to tumor development would be expected and, thus, studies that do not provide adequate follow-up can be misleading.

Among other groups of insulation workers, high rates of cancer, particularly bronchogenic carcinoma and pleural or peritoneal mesothelioma, have been reported by Selikoff (1976). In this study 632 New York and New Jersey insulation workers, 20 or more years from onset of exposure were observed from January 1, 1943 through December 31, 1974. Of these, fewer than 300 individuals were included in the larger study of 17,800 insulation workers. With a much longer observation period, even more severe effects were seen. Similarly, a study by Elmes and Simpson (1971, 1977) in the United Kingdom portrays a more severe mortality experience, particularly for lung cancer over a period of time, 1940-1975.

Some data on exposure of U.S. insulation workers exist. These have been reviewed by Nicholson (1976) and are summarized in Table 22. Estimates of past average exposures were made on the basis of current measurements by four laboratories of fiber concentrations during work activities thought to be typical of those of past years and information on product composition and usage. Time-weighted average concentrations of 10 to 15 f > 5 µm/ml and 15 to 20 f > 5 µm/ml were suggested for commercial construction and marine work, respectively. It was noted that, while these average concentrations were not extraordinary, peak concentrations could often be very high and exceed 100 f/ml. At Lyon, in 1972, Cooper and Miedema (1973) reported, "peak concentrations may be high for brief periods, while time-weighted averages are often deceptively low." To the extent possible these high exposures were taken into account and the time-weighted average exposure was largely due to peak exposures. This averaging and the extrapolation to earlier years introduce uncertainties in the estimate. However, the above

TABLE 22

Summary of Average Asbestos Air Concentrations during Insulation Work

	Average Fiber Concentration f/ml	
Research Group	Light and Heavy Construction	Marine Work
Average concentrations of fibers longer than 5 μm evaluated by membrane filter techniques and phase-contrast microscopy		
Nicholson (1971b)	6.3	
Balzer and Cooper (1968)	2.7	
Cooper and Balzer (1968)		6.6
Ferris, et al. (1971)		2.9
Harries (1971a,b)		8.9
Average concentrations of all visible fibers counted with a konimeter and bright-field microscopy		
Murphy, et al. (1971)		8.0
Fleischer, et al. (1946)		30-40
Estimates of past exposure based on current membrane-filter data		
Nicholson (1976)	10-15	

time-weighted average exposures are felt to be accurate within a factor of two. This is suggested by the good agreement among the exposure estimates and measurements of four different laboratories and by the good agreement of insulator dose-response data with that of other groups.

Factory Employment: An early study of workers from an asbestos products factory (Mancuso and Coulter, 1963) showed a significant excess in total mortality, with important contributions to excess death rates from asbestosis, cancer of the lung, bronchus, and trachea, and neoplasms of the digestive organs and peritoneum. In this latter group of deaths, an important factor was peritoneal mesothelioma. While in excess, increases in cancer of the esophagus, stomach, colon, and rectum did not have statistical significance. There was a consistent increase in the mortality rate with increasing length of employment in the asbestos industry for all causes of death and especially for malignant neoplasms and asbestosis.

Additional studies of factory employees (Enterline, et al. 1972; Henderson and Enterline, 1979) focused upon a group of retirees from several plants of a major asbestos products manufacturing company. It shows a similar pattern of mortality. Table 23 lists standard mortality rates (SMRs) by cause in two time periods. The usual asbestos cancers and asbestosis are seen as significant causes of death. Here, too, a correlation was found between total dust exposure and excess mortality for both malignant and nonmalignant disease. Table 24 lists the data for lung cancer and shows a linear relationship with exposure.

These authors (Enterline and Henderson, 1973) suggested earlier that crocidolite may have a higher carcinogenic potential (for lung) than amosite or chrysotile. The later analysis (Henderson and Enterline, 1979) shows that individuals in the textile departments of the company (chrysotile only)

TABLE 23

Observed Deaths and SMRs for Selected Causes of Death by Period of Follow-up for 1,075 Males Retiring from a U.S. Asbestos Company from 1941-67 and Followed through 1973[a]

Cause of Death	1941-1973		1941-1969		1970-1973	
	Observed Deaths	SMR	Observed Deaths	SMR	Observed Deaths	SMR
All causes	781	120.4	616	115.8	165	141.6
Cancer (140-205)[b]	173	159.0	138	154.5	35	179.5
Digestive (150-159)	55	137.8	46	136.1	9	147.5
Respiratory (162-163)	63	270.4	49	270.7	14	269.2
All other cancers	55	120.6	43	115.0	12	146.3
Stroke (330-334)	74	96.4	48	76.7	26	183.1
Heart disease (400-443)	321	106.5	269	108.4	52	97.7
Respiratory disease (470-527)	68	173.0	54	178.2	14	155.6
Pneumoconiosis and pulmonary fibrosis (523-525)	31	--	25	--	6	--
Asbestosis (523.2)	19	--	16	--	3	--
All other causes	113	92.5	96	94.6	17	82.5
Death certificates not located	32	--	11	--	21	--

[a] Henderson and Enterline, 1979

[b] Disease code

TABLE 24

Lung Cancer Mortality Rates According to Dust Exposure[a]

Cumulative Dust Exposure (mppcf[b] - years)	SMR
<125	197.9
125 - 149	180.0
250 - 499	327.6
500 - 749	450.0
750	777.8

---

[a] Henderson and Enterline, 1979

[b] Million particles per cubic foot

have a lower lung cancer SMR than those in the pipe department (chrysotile and crocidolite) for equal dust exposures. However, no conclusions could be drawn from an analysis of the mortality rates of all individuals exposed, or not exposed, to crocidolite. Since the follow-up of this population began only after the cohort members reached age 65, survivor effects may be of importance. For example, those individuals who smoke cigarettes and are thus at higher risk for lung cancer may be preferentially excluded by virtue of death before age 65 because of smoking-associated disease such as myocardial infarction. Further, the limited number of mesotheliomas (5 of 781 deaths) found in the latest followup of this group could be due to the high incidence of mesothelioma at age 50 to 65, 30 to 45 years from onset of first employment (see Figure 3). Mortality data were correlated with estimates of previous dust concentrations in terms of millions of particles per cubic meter of air (mppcf). No information was provided on possible fiber concentrations.

A study of the largest factory of the company studied by Enterline, et al. (1972), but not limited to retirees, shows a considerably different mortality pattern (Nicholson, 1976; Nicholson, et al. 1980b). All 689 maintenance and production employees on January 1, 1959, who were first employed at least 20 years earlier were followed through 1976. In this group, 274 deaths occurred, whereas 188.19 were expected. Fourteen pleural and 12 peritoneal mesotheliomas accounted for nearly 10 percent of the deaths, most occurring before age 65. A strong correlation with estimated dust exposure was seen in deaths from asbestosis, but not with the asbestos-related malignancies. Gastrointestinal cancer was especially high in the lowest of four dust categories (11 observed versus 3.15 expected) and only elevated slightly in the higher exposure categories. In the highest dust category, the textile mill, cancer was not dramatically increased, but 40 percent of the deaths were from asbestosis. Individuals in this department tended to die of nonmalignant disease before reaching the age of greatest risk for cancer.

A study by Weill, et al. (1979) of two asbestos cement product facilities has also been published. Here, the mortality experience of 5,645 employees was followed for at least 20 years. It shows excess mortality for lung cancer in the highest exposed groups but deficits of death from all causes (as great as 40 percent) in all categories. Of the group 3,854 (68 percent) were employed for less than 2 years. Thus, exposures were limited for the majority of the cohort members. Further, as most of the followup involved observations prior to 25 years from first exposure (18,117 person-years at risk <25 years from initial exposures versus 5,910 person-years >25 years), there was limited risk from asbestos disease in the group. Of most consequence, however, 25 percent of the cohort was untraced and all untraced were considered alive. This could explain the large mortality deficits in all categories other than lung cancer and invalidates the study for any use in establishing dose-response relationship.

A final significant U.S. factory study is that of Seidman, et al. (1979) which extends an earlier study (Selikoff, et al. 1972) and documents the experience of workers exposed only to amosite asbestos in the production of insulation materials, primarily for use aboard naval vessels. Overall mortality shows patterns similar to other heavily exposed groups, with 594 deaths observed versus 368.62 expected. Lung cancer was more than five times the number expected, and 16 deaths from mesothelioma occurred. Of particular importance in this study is the finding that individuals employed for periods less than 6 months had significant excess of lung cancer (Table 25). Gastrointestinal cancer was also elevated for those with exposures of

TABLE 25

Expected and Observed Deaths from Lung Cancer and Cancer of the Esophagus, Stomach, Colon, and Rectum in Workers Exposed to Amosite Asbestos (Followed 5 to 35 Years after Employment from 1941 to 1945)*

Length of Employment	Lung Cancer Expected	Observed	GI Cancer Expected	Observed
1 mo	1.6	4	1.4	2
1 mo	2.5	6	2.4	2
2 mo	2.4	8	2.6	3
3-5 mo	4.2	9	4.2	8
6-11 mo	3.2	12	3.2	1
1 yr	2.6	15	2.5	5
2+ yrs	6.0	39	6.4	7
Total	22.5	93	22.7	28

*Source: Seidman, et al. 1979

less than 6 months (15 observed versus 10.6 expected), but the difference did not have statistical significance. Further, there was not an increasing risk with time of employment as in the case with lung cancer.

Some data exist that would indicate the air concentrations of asbestos to which workers in a factory, which operated in Paterson, New Jersey, from 1941 through 1954, were exposed. Following cessation of operations there, two similar plants were opened elsewhere, using the same equipment and manufacturing the same product with the same materials. As in the Paterson factory, dust control was inadequate in the newer plants. These continued operation through 1971 in one case and 1975 in the second. During 1967, 1970, and 1971 asbestos fiber concentrations in the plants were measured by the National Institute for Occupational Safety and Health (NIOSH, 1972), and the results are presented in Table 26. The overall arithmetic average exposure was 34.9 f/ml with a range from about 20 to 80. Using 40 f/ml, as an estimate of the fiber count in the Paterson factory, one calculates the average dose received by those employed for less than 6 months to be no more than 120 f/ml-months, the same dose as would be received by a worker employed 20 years at an exposure of 0.5 f/ml. Of significance, also, is that the mesothelioma risk is less than that of insulators (3 percent versus 7 percent). Since times from onset of exposure to amosite are comparable for each group, the presence of amosite in insulation materials cannot explain the high rate of mesothelioma among insulators.

In Great Britain, a well-studied factory population (Doll, 1955; Knox, et al. 1968) provides useful information because of the availability of environmental information. The mortality experience of this group has been recently updated (Peto, et al. 1977). Workers exposed prior to 1933 (before dust concentrations were significantly reduced) had a marked excess of lung

TABLE 26

Asbestos Fiber Concentrations in Two Amosite Insulation Production Facilities[a,b]

ASBESTOS INSULATION PLANT Y

	1967		1970		1971	
Operation	Mean	No. of Samples	Mean	No. of Samples	Mean	No. of Samples
Mixing	107.0	3	27.7	2	46.3	7
Forming	98.9	12	24.1	13	25.2	32
Finishing	32.2	4	16.8	2	15.0	17
Inspection and Packing	13.3	2	13.0	8	11.0	19
Miscellaneous			21.0	14	2.7	5

ASBESTOS INSULATION PLANT X

	1967		1970		1971	
Operation	Mean	No. of Samples	Mean	No. of Samples	Mean	No. of Samples
Mixing	163.0	5	36.2	3	74.4	11
Forming	33.3	18	25.7	3	50.6	39
Curing	2.5	1	31.0	1	14.4	5
Finishing	44.6	3	34.8	4	39.5	26
Inspection and Packing	16.7	7	17.9	3	22.8	15
Miscellaneous			13.8	2	16.6	24

[a] NIOSH, 1972

[b] All samples expressed as $f > 5$ μm/ml.

cancer (25 observed versus 4.63 expected). Other cancers were elevated, but not so greatly. Of significance, however, individuals employed after 1933, and even after January, 1951, were found to have an excess risk of lung cancer. These data were analyzed by Peto (1978) in relation to measured and estimated fiber concentrations. Exposures averaged about 10 f/ml after 1933 and were virtually exclusively chrysotile. Using a linear dose-response relationship for lung cancer and pleural mesothelioma, he estimated that a 2 f/ml exposure for 50 years would cause approximately 10 percent of male asbestos workers to die from asbestos-related disease. It should be noted that data available for analysis were very limited and the estimate was based on extremely small numbers (14 deaths from lung cancer, 4 from mesothelioma, and 17 from nonmalignant respiratory disease). Furthermore, few individuals in the cohort were more than 35 years from onset of exposure and at a period of highest risk from asbestos disease.

Another factory population has been extensively studied (Newhouse, 1969; Newhouse, et al. 1972; Newhouse and Berry, 1976, 1979). Exposures were to chrysotile, crocidolite, and amosite. Table 27 lists the mortality experience of both men and women according to estimates of fiber exposure (no details are provided as to the method of estimation) (Newhouse and Berry 1979). Lung cancer, gastrointestinal cancer, and mesothelioma are significantly elevated in the long-term (>2 years) or severe exposure groups. It has been estimated (Newhouse and Berry, 1976) that as much as 11 percent of this entire group will die of pleural or peritoneal mesothelioma. Among female workers, cancer of the breast and cancer of the ovary were significantly higher ($p = 0.05$).

Mining and Milling: Three studies exist showing mortality patterns in the mining and milling of pure chrysotile asbestos. A series of studies

TABLE 27

Mortality Experience of Male and Female Factory Workers[a]

No. of Exposed Males	884		554		937		512	
	Low to Moderate (5-10 f/ml)				Severe (20+ f/ml)			
	<2 yrs		>2 yrs		<2 yrs		>2 yrs	
Cause of Death	0	E	0	E	0	E	0	E
All causes	118(4)	118.0	89(7)	95.3	162[d](16)	122.2	176[d](19)	102.5
Cancer of lung and pleura (ICD 162 -163)[e]	17(3)	11.01	16(1)	9.0	31[d](6)	12.8	56[d](7)	10.4
GI cancer (ICD 150-158)	10	9.0	9(4)	7.3	20[c](6)	9.5	19[c](8)	8.2
Other cancers	6	7.4	8(1)	5.8	16[c](3)	7.9	16[c](4)	6.3
Chr. resp. disease	19	17.5	16	14.7	20(1)	17.6	28	15.9

TABLE 27 (continued)

Mortality Experience of Male and Female Factory Workers[a]

No. of Exposed Females	98		396		199	
Cause of Death	Low to Moderate (5-10 f/ml)		<2 yrs	Severe (20+ f/ml)	>2 yrs	
	0	E	0	E	0	E
All causes	34[b](1)	22.0	88[c](13)	65.6	78[d](7)	30.4
Cancer of lung and pleura (ICD 162-163)	3[b](1)	0.5	15[d](7)	1.9	21[d](4)	0.8
GI cancer (ICD 150-158)	3	1.9	14[c](4)	5.7	9[c](2)	2.6
Other cancers	4	3.2	16(2)	11.9	16[d](1)	5.3
Chr. resp. disease	3	2.3	6	6.8	10[c]	3.2

[a] Newhouse and Berry, 1979

[b] $p < 0.05$

[c] $p < 0.01$

[d] $p < 0.001$

[e] Disease codes

Numbers in parentheses are mesotheliomas

(McDonald and Liddell, 1979; McDonald, et al. 1971, 1980) of 10,939 male Canadian mine and mill employees show excess mortality, particularly of the respiratory system. Table 28 lists the mortality for those individuals in the cohort that achieved 20 or more years from first employment. Standard mortality ratios were calculated from the expected number of deaths in the province of Quebec. The risk of death from lung cancer increases linearly with dust index with no evidence of a threshold [relative risk = 1 + 0.0014 (mppcf-years)]. The mortality for esophogeal and stomach cancers shows a strong relationship with dust index, but that of colonrectal cancer does not. Pleural mesothelioma was a cause of 11 deaths to 1975. The use of Quebec mortality statistics may underestimate the actual risk as the earliest report by McDonald (McDonald, et al. 1971) stated that lung cancer mortality in the five counties near the asbestos mines was only two-thirds of the province as a whole, the rates of which would be dominated by the urban center, Montreal. The effect of urban-rural difference on the rates of cancer at other sites is not known. Additionally, it is not stated in the publication how the 10 percent of the cohort that was untraced was treated. All data on exposure are given in terms of millions of particles per cubic foot (mppcf). While earlier work described the difficulties of converting particle counts to f/l (Gibbs and LaChance, 1974), it is now suggested that a conversion factor between 1 and 5 f/m per mppcf may be appropriate (McDonald, et al. 1980).

A Soviet study of the health effects of chrysotile mining and milling is that of Kogan, et al. (1972). Overall excess mortality of cancer of the respiratory or digestive tract was seen, particularly in the groups aged 50 years or older (and presumably 30 or more years from first exposure). Among these, stomach cancer mortality in male miners is increased 2.5 times and

TABLE 28

Dust Exposure and Mortality in Chrysotile Mining, 1910-75
Deaths, by Cause, in Relation to Duration of Service*

Cause of Death	Length of Service Very Short (<1) 0	SMR	Short (1 - <5) 0	SMR	Medium (5 - <20) 0	SMR	Long (>20) 0	SMR	Complete Cohort 0	SMR
All causes	885	1.07	629	1.09	679	1.15	1,098	1.07	3,291	1.09
Pneumoconiosis	1	1.15	3	5.00	2	3.39	36	34.62	42	33.55
Malignant neoplasms:										
Lung	47	0.97	29	0.83	50	1.37	104	1.61	230	1.25
Esophagus and stomach	37	1.30	25	1.27	18	0.91	50	1.47	130	1.27
Colon and Rectum	22	0.78	13	0.67	23	1.16	21	0.62	79	0.78
Other abdominal	20	1.08	12	0.92	14	1.04	21	0.90	67	0.98
Larynx	6	1.48	5	1.75	1	0.34	4	0.78	16	1.07
Other	67	1.12	43	1.04	48	1.13	79	1.08	237	1.09
Heart disease	370	1.06	251	1.02	287	1.15	424	0.97	1,332	1.04
Respiratory tuberculosis	7	0.62	7	0.89	21	2.68	22	1.56	57	1.39
Other respiratory	29	0.66	46	1.52	22	0.71	59	1.12	156	0.99
Cerebrovascular	62	0.95	49	1.12	50	1.13	82	1.11	243	1.07
Accidents	52	1.36	38	1.32	37	1.18	56	0.96	183	1.17
All other known causes	130	1.03	94	1.07	94	1.05	132	0.85	450	0.98
Cause not known	35	--	14	--	12	--	8	--	69	--

Columns headed with 0 give the numbers of deaths of men, 20 years or more after first employment, occurring during 1951-75; figures under headings SMR are ratios of deaths observed to those expected on basis of male mortality in Quebec.

*Source: McDonald, et al. 1980

that of female workers by 3.6 times. The corresponding increases for female and male mill workers are 4.3 and 19.9 times expected. Additionally, intestinal cancer is elevated among the 50+ year group 4.3 times for male miners, 6.9 times for female miners and 14.3 for women mill employees. Unfortunately, data on the number of deaths are not provided. No cases of mesothelioma are reported.

Anthophyllite mining has also been found to produce a high risk of bronchogenic carcinoma (Meurman, et al. 1974). In a study of miners exposed to fibers of cummingtonite-grunerite ore series (in which amosite is formed), Gillam, et al. (1976) reported excess malignant respiratory disease (10 observed versus 2.7 expected) at an average air concentration of 0.25 f/ml.

No cohort mortality studies exist for the mining or milling of crocidolite or amosite.

In the above studies of chrysotile mining and milling, mesothelioma was present to much less a degree than in the following three instances: a factory using chrysotile exclusively, (4 percent of 20+ year employees) (Peto, 1978); the largest U.S. chrysotile using facility (10 percent) (Nicholson, et al. 1979); or insulation work using chrysotile and amosite (7 percent) (Selikoff, et al. 1979a). It appears that as the fibers are manipulated through milling, processing, and use, their carcinogenic potential increases. Whether this is related to a reduction in fiber size or other factors is yet to be definitively established, particularly in view of animal data which indicates a reduction in carcinogenic potential following ball-milling (see Animal Inhalation section).

Because of its relevance to ingestion, a summary of the available data on gastrointestinal cancer and peritoneal mesothelioma is given in Table 29.

TABLE 29

Gastrointestinal Cancer in Occupationally Exposed Asbestos Workers

Reference	Years of Observation	Causes of Death (ICD)^a	Expected Deaths	Observed Deaths	Excess Deaths	SMR	Number of Peritoneal Mesotheliomas
			INSULATION WORKERS				
Selikoff, et al. (1979a)	1967-77	150-154	59.10	99	39.9	168	109
Selikoff (1976)	1943-74	150-154	13.63	43	29.4	315	22
Kleinfeld, et al. (1967)	1945-65	150-159				390^c	
Elmes and Simpson (1971)	1940-66	150-154	4-	12	8+	300+	3
			FACTORY WORKERS				
Henderson and Enterline (1979)	1941-74	150-159	40.1	55	14.9	137.8	few
Nicholson, et al. (1979b)	1959-76	150-154	7.99	15	7.0	188	12
Seidman, et al. (1979) (amosite only)	to 1977	150-154	21.55	32	10.5	149	8
Newhouse and Berry (1979) low-mod. exposure	to 1975	150-158	18.2	18	-0.2	99	5
severe exposure		(excluding mesothelioma)	26.0	42	16.0	162	30

TABLE 29 (continued)

Gastrointestinal Cancer in Occupationally Exposed Asbestos Workers

Reference	Years of Observation	Causes of Death (ICD)[a]	Expected Deaths	Observed Deaths	Excess Deaths	SMR	Number of Peritoneal Mesotheliomas
MINING AND MILLING							
McDonald and Liddell (1979) "heavy exposures"	to 74	150-151				289[b]	none
Kogan, et al. (1972)		150					
age 50+ male miners						250[b]	
male millers						430	none reported
female miners						360	
female millers						1,990	

[a] Disease codes

[b] No information on number of deaths

[c] Proportionate mortality

Indirect Occupational Asbestos Exposure: In 1968 it was pointed out by Harries (1968) that shipyard workers other than insulators were at risk from asbestos disease. Among Devonport Dockyard employees, five cases of mesothelioma were found among men who had not been "asbestos workers" but had followed other trades in the yard. These men presumably had been inadvertently exposed to asbestos merely by working in the same shipyard areas where asbestos had been used. Continuing to follow this group, Harries later documented 55 cases of mesothelioma in this shipyard alone, only 2 of which occurred in asbestos workers (Harries, 1976), and 1 of which occurred in a man who had previously sprayed asbestos. A study of the distribution of all verified cases of mesothelioma found in Scotland between the years of 1950 and 1967 is also revealing. Of 89 cases available for study, 55 were in shipyard employees, dockers, or naval personnel. Of the 55, again only 1 was an asbestos insulation worker (McEwen, et al. 1977).

A study by Edge (1976) of men who had worked in a shipyard in Barrow, England, attempted to establish a risk of low-level asbestos exposure on a population basis. He selected 235 shipyard workers with pleural plaques but no parenchymal fibrosis on X-ray, and followed their mortality experience from 1970 through 1973. Seventy died, 17 of mesothelioma and 13 from lung cancer, 2.6 times greater than expected. However, the relevance of these data have been called into question by the possibility of bias in the selection of the 235 cases (Edge 1979).

The previously mentioned radiological evidence (see Indirect Occupational Asbestos Exposure section) that asbestos concentrations in general shipyard work (Selikoff, et al. 1979a) or maintenance activities in a chemical factory (Lilis and Selikoff, 1979) are sufficient to produce fibrosis points to the existence of a widespread carcinogenic problem from indirect asbestos exposures.

Environmental Asbestos Disease: Wagner, et al. (1960) reviewed 47 cases of mesothelioma found in the Northwest Cape Province, South Africa in the previous 5 years. Of this number, roughly half the cases were in people who had worked with asbestos. Virtually all the rest were in individual who had, decades before, simply lived or worked in an area of asbestos mining (one living along a roadway in which asbestos fibers were shipped). This germinal observation demonstrated that asbestos exposure of limited intensity, often intermittent, could cause mesothelioma. The hazard was further pointed out by the findings of Newhouse and Thomson (1965), who showed that mesothelioma could occur among people whose potential asbestos exposure consisted of their having resided near an asbestos factory or in households of asbestos workers. Twenty of 76 cases from the files of the London Hospital (1917 to 1964) were the result of such exposure; 31 were occupational in origin, and asbestos exposure was not identified for 25.

Both pleural and peritoneal mesotheliomas have been found to occur from environmental asbestos exposure. For example, in the neighborhood and family cases documented by Lieben and Pistawka (1967), two of three family contacts and two of eight neighborhood mesotheliomas were peritoneal. In general, a greater percentage of environmental mesotheliomas compared to occupational are pleural in origin. This, however, may be the result of a greater propensity for peritoneal mesotheliomas to be misdiagnosed. In occupational circumstances, 40 percent of pleural mesotheliomas were correctly classified on death certificates versus only 21 percent of peritoneal mesotheliomas (Selikoff, et al. 1979a).

Synergism and/or Antagonism

Asbestos exposure and cigarette smoking have been found to act synergistically to produce dramatic increases in lung cancer over that from exposure to either agent alone. In a prospective study by Hammond, et al. (1979) of 17,800 insulation workers, smoking histories were solicited from all individuals during 1966 prior to observation. Of 12,051 workers who passed the 20-year point since entering the trade before or during the 10-year observation period, January 1, 1967 to December 31, 1976, 891 reported they had never smoked, 488 had smoked only a pipe and/or cigars, and 6,841 gave a history of cigarette smoking. No information was available from the remaining 3,831. Using data of the American Cancer Society (ACS) on age- and calendar year-specific cancer rates among smokers and nonsmokers in a prospective study of more than one million people in the United States, it was possible to make smoking-specific comparisons of the mortality experience of insulation workers with nonasbestos exposed individuals in the general population. Those insulation workers who claimed never to have smoked cigarettes were found to have an increased risk of death from lung cancer compared with nonsmokers in the general population, although there were relatively few deaths, 8 observed versus 1.3 expected. However, among those with a history of cigarette smoking, the risk was also increased and its effect was large, 268 deaths being recorded versus 4.7 expected. Among noncigarette smokers in the general population Table 30 lists the death rates and mortality ratios of smoking and nonsmoking asbestos workers compared to the ACS control population. Asbestos exposure appears to multiply the risk of death of lung cancer by four to six times, irrespective of smoking habits. When that risk is already high, as in cigarette smokers, the result is catastrophic. An earlier study by Selikoff, et al. (1968) indicated that the risk of death from lung cancer in cigarette-smoking asbestos workers was 92 times that among individuals who were neither exposed to the fiber nor smoked cigarettes.

TABLE 30

Age-Standardized Lung Cancer Death Rates[a] For Cigarette Smoking and/or Occupational Exposure to Asbestos Dust Compared with No Smoking and No Occupational Exposure to Asbestos Dust[b]

Group	Exposure to Asbestos	History Cigarette Smoking	Death Rate	Mortality Difference	Mortality Ratio
Control[c]	No	No	11.3	0.0	1.00
Asbestos workers	Yes	No	58.4	+47.1	5.17
Control	No	Yes	122.6	+111.3	10.85
Asbestos workers	Yes	Yes	601.6	+590.3	53.24

[a] Rate per 100,000 man-years standardized for age on the distribution of the man -years of all the asbestos workers. Number of lung cancer deaths based on death certificate information.

[b] Hammond, et al. 1979.

[c] The central population is a group of 73,763 white, male workers exposed on the job to dust, fumes, vapors, chemicals, or radiation.

Cancers of the larynx, pharynx and buccal cavity, and of the esophagus in insulation workers are also associated with cigarette smoking (Hammond, et al. 1979). Among 50 deaths due to tumors of these sites, none were among nonsmokers and 3 were among individuals who smoked only pipes or cigars. Mesothelioma of the pleura or peritoneum and cancer of the stomach, colon, and rectum, however, were unrelated to smoking habits. It is worth noting that in these studies by Selikoff and Hammond over 200 excess deaths occurred from peritoneal mesothelioma and gastrointestinal cancer (excluding esophagus) in 2,271 deaths of insulation workers. Were smoking-related lung cancer not a factor, abdominal cancer deaths would dominate the mortality experience of this group of asbestos workers.

Other studies have substantiated the synergistic effect of cigarette smoking. Berry, et al. (1972) obtained retrospective smoking histories on a group of asbestos workers and analyzed their mortality according to smoking habits over a 10-year period of time. The results indicated that the combined effect of cigarette smoking and asbestos exposure on the development of lung cancer is multiplicative rather than additive.

Although synergistic effects have been documented for bronchogenic carcinoma, only cigarette smoking has been investigated in the etiology of abdominal cancers. The possibility exists, of course, that these tumors too could have a multiple factor etiology and that other contaminants, ingested with asbestos, may potentiate tumor development.

Additionally, some nonmalignant asbestos effects are related synergistically to cigarette smoking. Among a group of factory employees it was found by Weiss (1971) that evidence of fibrosis, as manifest on X-rays, was increased among individuals who smoked cigarettes compared to nonsmokers. Deaths due to asbestosis appear also to be increased in cigarette smokers compared to nonsmokers (Hammond, et al. 1979).

In animal experiments, exposure to benzo(a)pyrene (BP) and asbestos may act synergistically. Pylev and Shabad (1973) reported that intratracheal injections of 6 mg of chrysotile onto which was absorbed 0.144 mg of BP (from a benzene suspension) and 2 mg of chrysotile coadministered with 5 mg BP produced malignant tumors in 29 percent and 54 percent of rats, respectively. Administration of 6 mg of chrysolite or 5 mg BP yielded no tumors. Miller, et al. (1965) found intratracheal injection of chrysolite with BP to increase tumor yield over that of BP alone while amosite appeared to have little such effect.

No data exist on antagonistic or prophylatic compounds in relation to animal or human disease. *In vitro* experiments by Schnitzer, et al. (1971) have shown that hemolysis of red cells can be inhibited by coating the fibers with ionic polymers such as carboxymethylcellulose.

Fiber Size Considerations

Experimental systems, particularly those used by Stanton and Wrench (1972) and Pott, et al. (1976), indicate a significantly reduced carcinogenicity of fibers as the length is reduced or the diameter increased. On the other hand, human data suggest an important role for small fibers. From analyses of tissue samples from 29 mesothelioma cases, Sebastien, et al. (1979) found that larger fibers, often amphiboles, tend to be found in the lung parenchyma. In contrast, in the pleura, the fibers were finer and shorter and generally chrysotile. The mean length in pleura was 2.3 μm and that of the lung 4.9 μm. In 20 pleural samples of 29 autopsy cases in which asbestos fibers were found, chrysotile was identified as the only fiber in 8 and only a trace (<1 percent) of amphiboles was found in 2 others. In contrast, significant percentages of amphibole fibers (>18 percent) were found in 26 of 29 lung parenchyma samples from the same cases.

In an examination of the mortality of workers in different types of asbestos industries, significant differences occur that may be related to fiber size. In amosite and chrysotile mining, few mesotheliomas are seen, whereas, in manufacturing and end product use, large percentages of deaths occur from this tumor. For example, chrysotile mining and milling, while related to a significantly increased risk of death from lung cancer and asbestosis (McDonald and Liddell, 1979; Nicholson, et al. 1979), has not been associated with an extraordinary mesothelioma risk. Similarly, amosite mining and milling does not appear to significantly increase the risk of mesothelioma, while crocidolite mining and milling does (Webster, 1970). On the other hand, the manufacture of amosite products is associated with a significant risk of death from mesothelioma, 3.5 percent of the deaths of individuals 20 or more years from first employment being from this cause (Seidman, et al. 1979). Further, insulators who were exposed to chrysotile and amosite, but never to crocidolite (Selikoff, et al. 1970) have 9 percent of their deaths, 20-plus years from onset of exposure, from mesothelioma (Selikoff, et al. 1979a). As neither amosite nor crocidolite can account for this extraordinary risk, chrysotile must contribute significantly. This is also borne out by observations of the mortality of workers in a chrysotile using factory. 4.3 percent of long-term deaths were from mesothelioma in a facility using 5,000-6,000 tons of chrysotile, approximately 50 tons of amosite, and less than 4 tons of crocidolite annually (except for 3 years when 375 tons of amosite were used annually) (Robinson, et al. 1979).

Much of these differences in risk may be accounted for by the differences in fiber size distributions in the three work environments rather than by fiber type. The greatest percentage of longer and thicker fibers would occur in the work environment of miners and millers. As the asbestos is used in manufacturing processes, it is broken apart as it is incorporated in finished products. During application or removal of insulation products, it is further manipulated and the fiber reduced in length and diameter. As these smaller fibers can readily be carried to the periphery of the lung, penetrate the visceral pleura and lodge in the visceral or parietal pleura, they may be of greater importance in the etiology of mesothelioma, even though longer fibers, once there, are more carcinogenic. In the case of crocidolite, fine fiber aerosols are produced even in mining and, thus, all uses of that fiber are associated with mesothelioma.

CRITERION FORMULATION

Existing Guidelines and Standards

The current Occupational Safety and Health Administration (OSHA) standard for an 8-hour time-weighted average (TWA) occupational exposure to asbestos is 2 fibers longer than 5 microns in length per milliliter of air (2 f/ml or 2,000,000 f/m^3). Peak exposures of up to 10 f/ml are permitted for no more than 10 minutes (29 CFR 1910.001). This standard has been in effect since July 1, 1976, when it replaced an earlier one of 5 f/ml (TWA). In Great Britain, too, a value of 2 f/ml is the accepted level, below which no controls are required (BOHS, 1968); the British standard, in fact, served as a guide for the OSHA standard (NIOSH, 1972).

The British standard was developed specifically to prevent asbestosis among working populations; data were felt to be lacking that would allow a determination of a standard for cancer (BOHS, 1968). Unfortunately, among occupational groups, cancer is the primary cause of excess death among workers (see Carcinogenicity section). Three-fourths or more of asbestos-related deaths are from malignancy. This fact has led OSHA to propose a lower TWA standard of 0.5 f/ml (500,000 f/m^3) (29 CFR 1910.001). The National Institute for Occupational Safety and Health (NIOSH), in their criteria document for the hearings on a new standard, have proposed a value of 0.1 f/ml (NIOSH, 1976). In the discussion of the NIOSH proposal, it was stated that the value was selected on the basis of the sensitivity of analytical techniques using optical microscopy and that 0.1 f/ml may not necessarily protect against cancer. Recognition that no information exists that would define a threshold for asbestos carcinogenesis was also contained in the preamble to the OSHA proposal. The existing standard in Great Britain has also been called into question by Peto (1978), who estimates that asbestos disease may cause the death of 10 percent of workers exposed at 2 f/ml for a working lifetime. A fiber concentration limit of 1.0 f/ml has recently been published in Great Britain (Advisory Committee on Asbestos, 1979).

The existing Federal standard for asbestos emissions into the environment prohibits "visible emissions" (40 FR 48291). No numerical value was specified because of difficulty in monitoring ambient air asbestos concentrations in the ambient air or in stack emissions. (Time-consuming and expensive electron microscopy is often required.) Some local government agencies, however, may have numerical standards (New York, 27 ng/m^3 for example).

No standards for asbestos in foods or beverages exist even though the use of filtration of such products through asbestos filters has been a common practice in past years. Asbestos filtration, however, is prohibited or limited for human drugs (41 FR 16933).

Current Levels of Exposure

As detailed in the Exposure section, asbestos is a ubiquitous contaminant of our air and water. Air concentrations over 24 hours in metropolitan areas usually are less than 5 ng/m^3 but can range up to 20 ng/m^3. Values up to 50 ng/m^3 are found during daytime hours in locations where construction activities and traffic can be contributing sources. A significant fraction of the fibers inhaled can be brought up from the respiratory tract and swallowed. This leads to an ingestion exposure from air sources of up to 0.1 µg/day, although most of the population exposure is from 0.01 to 0.05 µg/day.

Water concentrations of asbestos are usually less than 10^6 fibers of all sizes per liter although significantly higher values (10^8 f/l) have been found in circumstances where water systems have been in contact with asbestiform minerals or where contamination of the water supply exists. Fiber mass concentrations corresponding to fiber concentrations are usually less than 0.01 µg/l but could exceed 1 µg/l. Thus, direct water ingestion usually leads to exposures of less than 0.02 µg/day.

Clearly, point source pollution can cause both air and water concentrations to exceed the above values. Such instances are discussed in the Exposure section.

Special Groups at Risk

Special groups at risk may include neonates and children; however, no data exist on the relative sensitivity to asbestos of infants and children undergoing rapid growth. Concern exists because fibers deposited in the tissues of the young may have an extremely long residence time during which malignant changes could occur. In addition, risk could be influenced by differential absorption rates which have not been fully studied at this time.

Individuals on kidney dialysis machines may also be at greater risk as fluids, potentially contaminated with asbestos fibers can enter the blood stream directly or, in selected instances, the peritoneal cavity (peritoneal dialysis).

Although no synergistic effects have been identified in the etiology of asbestos-related gastrointestinal cancer, they cannot be ruled out. Thus, people exposed to other carcinogens, initiators, or promotors could be at increased risk.

An increased risk is also associated with increased exposure to asbestos in water in municipalities such as San Francisco or Seattle where asbestos occurs naturally in water, in cities where there is an interaction between aggressive water and asbestos-cement pipe, or in cities whose water may be contaminated as a result of asbestos operations. Also, the use of asbestos cement products for the collection of water, such as in cisterns in the Virgin Islands or in roof run-offs in tropical areas, increases exposure.

Basis and Derivation of Criterion

As previously discussed, no definitive studies, either animal or human, exist that would establish risk levels from ingestion of asbestos fibers. Those studies published provide both positive and negative data, but all have methodological limitations. In the case of the human studies, these include observations on only recently exposed individuals, small study groups, low exposures, population mobility, uncertainty over the effect of confounding variables, and inappropriate control populations. Animal studies have usually been conducted with very small numbers of animals, have lacked proper pathology, used limited doses of asbestos, and poorly defined the materials ingested.

On the other hand, human studies of workers exposed to airborne asbestos unequivocally demonstrate an excess risk of gastrointestinal cancer in virtually all groups surveyed. A route of exposure to the gastrointestinal tract from such exposures is also clear from the fibers cleared from the lung and bronchial tract and subsequently swallowed. Using information on airborne exposures to workers, it is possible to estimate an approximate exposure level to the gastrointestinal tract from estimates of airborne asbestos concentrations. This, however, involves the use of data having, in some cases, significant uncertainties and, thus, the criterion level on asbestos in water that will produce a specified risk cannot be established with high precision.

Experimental uncertainties exist as to the air concentrations in fibers longer than 5 μm/ml to which workers were exposed in past years, the conversion of these >5 μm fiber concentrations to concentrations of fibers of all sizes in air, and on the size distributions of water and airborne asbestos sols. Information is also lacking on the importance of fiber size in the production of human cancer. On the one hand, longer fibers are more carcinogenic in experimental systems although quantitative data are limited. On the other hand, smaller fibers appear to more readily cross body barriers to reach sites of importance for human carcinogenesis. The relative importance of these two factors cannot be accurately estimated.

A substantial body of data exists which shows increased incidence of cancer of the esophagus, stomach, colon, and rectum or peritoneal mesothelioma in humans exposed to asbestos occupationally. For several of these groups, data exist on the approximate airborne fiber concentrations to which individuals were exposed (see Effects section). These human data will serve as the primary basis for a standard of asbestos in water. Experimental data (see Pharmacokinetics section) indicate that a major fraction of the asbestos deposited in the lungs is subsequently swallowed. In this section, the dose to the gastrointestinal tract of four occupational groups will be calculated from knowledge of the air concentrations to which the workers were exposed and the assumption that all the asbestos inhaled subsequently passed through the gastrointestinal tract and provided the exposure that led to the observed increase in abdominal cancer. The assumption that all inhaled asbestos is ingested is an overestimate but not a significant one. No account has been taken of the material that a worker may swallow directly, and this quantity could be important. The extent to which these factors are offsetting cannot be estimated. Uncertainties exist in the extrapolation of animal data on clearance to man and in the effect of the aerosol size distribution on the fraction swallowed. These uncertainties, however, are felt to be unimportant in comparison to our inability to estimate the quantity of asbestos that might be directly swallowed. If the amount of asbestos directly ingested is less than that which remains in the lungs or is cleared from the body by other than ingestion, the estimated criteria level will be less stringent. If the directly ingested asbestos is of more importance, the criteria level will be more stringent.

Table 31 lists the percentage of death from excess gastrointestinal cancer and peritoneal mesothelioma in four groups of asbestos workers. Calculations of these percentages were made using expected numbers of death, rather than the observed, because the latter is often significantly inflated by including other asbestos-related deaths (asbestosis, lung cancer, and pleural mesothelioma).

Table 32 lists the fiber concentration estimates (see Carcinogenicity section) and an exposure index for each cohort (years of exposure x fiber concentration). This index will be used to calculate the number and mass of asbestos fibers ingested during a working lifetime. As the observed mortality is, to a large extent, after 20 years from first exposure, the intermixing of time and exposure does not present significant problems.

The average length of exposure for the insulation workers in the first group was calculated from data on employment time at entry into the cohort in 1967. A working lifetime of 40 years was used for the smaller group of New York and New Jersey insulators, virtually all of whom were deceased or retired. The estimate of the person-weighted exposure index for the amosite factory is simply the average employment time multiplied by 40 f/ml. Data from Table 33 were used to estimate a person-weighted exposure index for the Newhouse and Berry group.

[Person-weighted exposure index $= \frac{\sum(\text{No. at risk x exposure x time})}{\sum(\text{No. at risk})} = 180.$]

TABLE 31

Percentage of Excess Gastrointestinal Cancers and Peritoneal Mesotheliomas in Four Groups of Asbestos Workers

Exposed Group	Number of Excess Deaths (from Table 29) GI Cancer	Peritoneal Mesothelioma	Expected Number of Deaths in Cohort	Excess deaths as a Percentage of Expected Deaths in Cohort GI	Per. meso.	Total
Insulation workers[a] (chrysotile and amosite)	39.9 (ICD 150-154)	112	1,658.9	2.4	6.7	9.1
Insulation workers[b] (chrysotile and amosite)	29.4 (ICD 150-154)	22	305.20	9.6	7.2	16.8
Factory employment[c] (amosite)	10.5 (ICD 150-154)	8	368.62	2.9	2.2	5.1
Factory employment[d] (chrysotile, crocidolite and amosite)	15.8 (ICD 150-158 ex meso)	35	556.0	2.8	6.3	9.1
Factory Retirees[e] (chrysotile, crocidolite and amosite)	14.9 (ICD 150-159)	unknown but < 5	648.7	2.3	?	2.3
Miners and millers[f] (chrysotile)	27.8 (ICD 150-151)	0	3,019.3	0.9	0	0.9

[a] Selikoff, et al. 1979a

[b] Selikoff, 1976

[c] Seidman, et al. 1979

[d] Newhouse and Berry, 1979

[e] Henderson and Enterline, 1979

[f] McDonald, et al. 1980

TABLE 32

Exposure Indices for Asbestos Worker Groups

Exposed Group	Air Fiber Concentration (f/ml)	Person-weighted Average Exposure Time (yrs.)	Exposure Index (years x f/ml)
U.S. insulators Selikoff, et al. (1979a)	15 (Table 22)	34	510
NY/NJ insulators Selikoff (1976)	15 (Table 22)	40	600
Amosite factory workers Seidman, et al. (1979)	40 (Table 26)	1.9	76
British factory workers Newhouse and Berry (1979)	10-30	See Table 33	180
Factory retirees Henderson and Enterline (1979)	See note a		740
Chrysotile miners and millers	See note a		585

[a] The cumulative exposure index in f/ml x years was calculated by multiplying a person-weighted exposure index in mppcf x years by 3.

TABLE 33

Exposure Estimates for Workers in a British Factory*

Exposure Group		No. at Risk	Exposure (f/ml)	Time of Exposure (years)
Severe	<2 years	711	30	20
	>2 years	1,333	30	2
Low to Moderate	<2 years	503	10	20
	>2 years	933	10	2

*Source: Newhouse and Berry, 1979

The fiber exposures for the studies of McDonald, et al. (1980) and Henderson and Enterline (1979) were calculated from the estimate of McDonald, et al. (1980) that 1 mppcf is equivalent to 3 f/ml. While no data support this suggestion, it appears reasonable and was also used for the factory exposure circumstances.

The majority of samples analyzed for the EPA to date were characterized by a concentration of all electron microscopic visible fibers per liter of water (see Exposure section). Further, techniques for the determination of fiber concentrations (as opposed to mass concentrations) have been published as interim EPA procedures (Anderson and Long, 1980). Thus, a criterion for the concentration of fibers of all sizes in water corresponding to a 10^{-5} risk will be calculated directly from the concentrations of fibers greater than 5 μm measured in the occupational circumstances that produced disease. Unfortunately, the data currently available relating air concentrations of fibers longer than 5 μm, counted by optical microscopy, to those determined by electron microscopy, are extremely limited. These include those by Wallingford (1978), 1:15; Millette (personal communication), 1:400; and Winer and Cossett (1979), 1:1,000 and are only for chrysotile asbestos. Using the geometric mean of 200 for this factor from all available data, a total fiber concentration corresponding to a 10^{-5} risk can be calculated from the data of Tables 31 and 32. The scant data on the relation between electron and optical microscopic counts is uncertain. The variability between these three measurements is likely the result of losses during the preparation of specimens for electron microscopy. Thus, the value by Wallingford appears unduly low and is in disagreement with electron microscopic size distributions showing 1 to 3 percent of fibers in chrysotile asbestos aerosols to be longer than 5 μm. With these considerations, the uncertainty in the value 200 may be estimated to be a factor of 3.

In making the calculation, one tacitly assumes the same fiber size distribution in water as in occupational air samples. Some data show that water fiber size distributions vary greatly (Millette, et al. 1979a,b), and occupational air distributions have been shown to be so variable that the fraction of fibers longer than 5 μm can range over a factor of 10 depending on sampling circumstances (Nicholson, et al. 1972). Although sizing of airborne and waterborne fibers has not been done using the same methods, qualitatively, water appears to have fiber distributions with more smaller fibers than in occupational air samples. Experimental studies, previously discussed, have shown that once in place, longer fibers are more carcinogenic than shorter ones. However, shorter fibers appear to more easily cross organ barriers and migrate throughout the body, and may, thus, be of greater importance for some asbestos malignancies, particularly mesothelioma (Sebastien, et al. 1979). The extent to which the assumption of the same fiber size distribution in water as in air will likely yield a conservative criteria (from the point of view of health) cannot be estimated.

A detailed calculation of the 70-year lifetime risk from the injection of 10^6 fibers of asbestos per day is given in Appendix I. Data of the occupational risk of both gastrointestinal cancer and peritoneal mesothelioma were used (Table 31). Account was taken of the fact that occupational exposures took place over a 5-day work week and that the ingestion exposure may encompass a lifespan of 70 years. It was assumed that a worker breathes at the rate of 1 m^3/hr during work exposure for the purpose of calculating total asbestos intake per day. Using a linear dose-response relationship and a specified risk of 10^{-5}, the calculated 70-year daily intake resulting from these calculations are given in Table 34. It is not correct to simply average intake levels (rather than risks) as a single study showing

TABLE 34

The Calculated Risk of Death over a 70-Year Lifetime from Gastrointestinal Cancer and Peritoneal Mesothelioma from Ingestion of 10^6 f/day of Asbestos

Exposure Group	Estimated Risk / 10^6 f/day
Selikoff, et al. (1979a)	1.1×10^{-5}
Selikoff (1976)	1.7×10^{-5}
Newhouse and Berry (1979)	3.1×10^{-5}
Henderson and Enterline (1979)	1.9×10^{-6}
McDonald, et al. (1980)	9.5×10^{-7}
Average	1.24×10^{-5}

This average corresponds to a daily intake of 800,000 fibers for a 10^{-5} lifetime risk.

very low risks could yield an intake level of unlimited magnitude. The inclusion of such a level in any averaging process would clearly not be appropriate. The data from Seidman, et al. (1979) were not used because it was exclusively from amosite exposures. While exposure over the last 10 or 20 years of life may not have been of great importance in the generation of asbestos related cancers, those ingested during the first 10 years may be much more important than fibers ingested later, and no consideration was taken of this possibility in establishing criteria levels. Further, the occupational exposures from which the criteria were developed utilized exposures through the lifetime of the populations. Assuming that two liters of water are ingested per day, this would correspond to a concentration of 400,000 fibers of all sizes/liter of water.

It is remarkable that three long exposure groups had similar exposure indices. This would suggest that these estimates are indeed reasonable. The exposure index for the study of Newhouse and Berry may be low, and this would produce a higher risk estimate. On the other hand, as previously discussed, the mortality data of Henderson and Enterline (1979) and McDonald, et al. (1980) may underestimate effects producing lower risk estimates.

A criterion for a mass concentration of asbestos can also be calculated using the conversion value of 30 $\mu g/m^3/f/ml$ derived from the data of Table 2 for predominantly chrysotile exposures. A value of 150 $\mu g/m^3/f/ml$ for amosite appears more appropriate, based on the finding of Davis, et al. (1978) that amosite has approximately a three time greater conversion factor than chrysotile. A detailed calculation is given in Appendix II and the results summarized in Table 35. Assuming that 2 liters of water are ingested per day, a risk of 10^{-5} would be produced from ingesting water containing 0.05 ug/liter. As mentioned in the "Exposure" section, the variability

TABLE 35

The Calculated Risk of Death over a 70-Year Lifetime from Gastrointestinal Cancer and Peritoneal Mesothelioma from Ingestion of 1 μg/day of Asbestos

Exposure Group	Estimated Risk / μg asbestos
Selikoff, et al. (1979a)	7.3×10^{-5}
Selikoff (1976)	1.1×10^{-4}
Seidman, et al. (1979)	5.5×10^{-5}
Newhouse and Berry (1979)	2.1×10^{-4}
Henderson and Enterline (1979)	1.3×10^{-5}
McDonald, et al. (1980)	6.4×10^{-6}
Average*	8.6×10^{-5}

*This corresponds to a daily intake of 0.12 μg for a 10^{-5} lifetime risk.

in the data used to convert optical fiber counts to mass (factor D in Appendix II) leads to a large uncertainty (a factor of 5) in the above estimate.

Considering chrysotile and depending on the source of the asbestos in water (see Table 5), 0.05 µg/liter corresponds to from 10^6 to 25×10^6 fibers of all lengths per day. Such estimates are considerably higher than those derived previously and are most likely a reflection of the differences in the sizes of the fibers found in water, as compared to those found in air. Because of these uncertainties, high priority should be given to obtaining accurate size and mass distribution of typical fibers found in different circumstances (air and water) which would allow appropriate conversions to be made between fiber concentrations in air and water.

Although positive animal experiments had various experimental limitations, risk estimates were calculated from their data using a modified one hit model as previously discussed in the Methodology document. The data are presented in Table 36. Considering the large number of experimental uncertainties, these values provide reasonable support for the concentration derived from human exposure data.

This document was concerned with the estimation of that concentration of asbestos in water which will produce a lifetime risk of 1 in 100,000 in a population exposed continuously. The risk estimate was made using a linear extrapolation from existing human data and would appear to constitute a conservative extrapolation. However, in the case of asbestos, the risk factor of 1/100,000 is not conservative. If we were concerned with intermittent or localized contamination incidents of some carcinogen that once identified, could be abated, such a value would have utility. With asbestos, however, we are concerned with a ubiquitous contaminant in the environment to which large populations are continuously exposed for decades. Further, the estimated value has a high degree of uncertainty associated with it, based upon the data from which it was derived.

TABLE 36

Risk Estimates from Animal Experiments*

Effect	Estimated 10^{-5} Dosage (μg/l)
4/42 Kidney carcinomas 0/49 control	3.2
12/42 Malignancies 2/49 control	1.1

*Source: Gibel, et al. 1976

Under the Consent Decree in NRDC v. Train, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." Asbestos is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of asbestos in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and states in the possible future development of water quality regulations, the concentrations of asbestos corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of 1 additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates 1 additional case of cancer for every million people exposed, and so forth.

In the Federal Register notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, 10^{-6}, or 10^{-7} as shown in the following table.

Exposure Assumption	Risk Levels and Corresponding Criteria (1)		
	10^{-7}	10^{-6}	10^{-5}
2 liters of drinking water	3,000 f/1*	30,000 f/1	300,000 f/1
Consumption of fish and shellfish only		No Criterion	

*f = fibers

(1) Calculated by applying a relative risk epidemiological model as described in the Methodology Document to the human epidemiological data presented in Appendix III. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

Concentration levels were derived assuming a lifetime exposure to various amounts of asbestos occurring from the consumption of drinking water only.

Although total exposure information for asbestos is discussed and an estimate of the contributions from other sources of exposure can be made, this data will not be factored into ambient water quality criteria formulation until additional analysis can be made. The criteria presented, therefore, assume an incremental risk from ambient water exposure only.

REFERENCES

Advisory Committee on Asbestos. 1979. Vols. I and II: Final report of the Advisory Committee. Health and Safety Commission. Her Majesty's Stationery Office, London.

Amacher, D.E., et al. 1975. The dose-dependent effects of ingested chrysotile on DNA synthesis in the gastrointestinal tract, liver, and pancreas of the rat. Environ. Res. 10: 208.

Anderson, C.H. and J.M. Long. 1980. Interim method for asbestos in water. EPA 600/4-80-005. U.S. Environ. Prot. Agency Res. Lab., Athens, Georgia.

Anderson, H.A., et al. 1976. Household-contact asbestos neoplastic risk. Ann. N.Y. Acad. Sci. 271: 311.

Auribault, M. 1906. Bull. del-inspect. du travail.

Bader, M.E., et al. 1961. Pulmonary function in asbestosis of the lung on alveolar-capillary block syndrome. Am. Jour. Med. 30: 235.

Balzar, J.L. and W.C. Cooper. 1968. The work environment of insulating workers. Am. Ind. Hyg. Assoc. 29: 222.

Beaman, D.R. and D.M. File. 1976. Quantitative determination of asbestos fiber concentrations. Ann. Chem. 48: 1.

Berry, G., et al. 1972. Combined effect of asbestos exposure and smoking on mortality from lung cancer in factory workers. Lancet. 2: 476.

Bonser, G.M. and D.B. Clayson. 1967. Feeding of blue asbestos to rats. Br. Empire Cancer Campaign for Research. 45: 242.

Brain, J.D. and P.A. Volberg. 1974. Models of lung retention based on ICRP task group report. Arch. Environ. Health. 28: 1.

British Occupational Hygiene Society. 1968. Hygiene standard for chrysotile asbestos dust. Ann. Occup. Hyg. 11: 47.

Brown, A.L., et al. 1976. The reliability of measures of amphibole fiber concentration in water. Environ. Res. 12: 150.

Buelow, R.W., et al. 1980. The behavior of asbestos-cement pipe under various water quality conditions: A progress report. Res. Tech. Feb: 91.

Carter, R.E. and W.G. Taylor. 1980. Identification of a particular amphibole asbestos fiber in tissues of persons exposed to a high oral intake of the mineral. Environ. Res. 21: 85.

Chamberlain, M. and E.M. Tarmy. 1977. Asbestos and glass fibres in bacterial mutation tests. Mutat. Res. 43: 159.

Chatfield, E.J., et al. 1978. Preparation of water samples for asbestos fiber counting by electron microscopy. U.S. Environ. Prot. Agency. EPA 600/4-78-011.

Chopra, K.S. 1978. Interlaboratory measurements of amphibole and chrysotile fiber concentration in water. Jour. Test. Eval. 6: 241

Commins, B.T. and G.W. Gibbs. 1969. Contaminating organic material in asbestos. Br. Jour. Cancer. 23: 358.

Cook, P.M. 1978. Amphibole Fiber Concentration Determination for Series of Communication Air Samples: Use of X-ray Diffractions to Supplement Electron Microscope Analysis. *In*: P.A. Russell and A.E. Hutchins (eds.), Proc. Symp. Electron Microscopy and X-ray Applications to Environ. and Occup. Health Analyses. Ann Arbor Science Publishers, Ann Arbor, Michigan. p. 107.

Cook, P.M. and G.F. Olson. 1979. Ingested mineral fibers: Elimination in human urine. Science. 204: 195.

Cook, P.M., et al. 1974. Asbestiform amphibole minerals: Detection and measurement of high concentrations in municipal water supplies. Science. 185: 853.

Cook, P.M., et al. 1976. X-ray Diffraction and Electron Beam Analysis of Asbestiform Minerals in Lake Superior Waters. *In*: Proc. Int. Conf. Environ. Sensing Assessment. 34: 1.

Cook, P.M., et al. 1978. Evaluation of cartridge filters for removal of small fibers from drinking water. Jour. Am. Water Works Assoc. 70: 459.

Cooper, R.C. and W.C. Cooper. 1978. Public health aspects of asbestos fibers in drinking water. Jour. Am. Water Works Assoc. 72: 338.

Cooper, R.C., et al. 1978. Asbestos in domestic water supplies for five California counties. Progress report for period April 25, 1977 to June 30, 1978, under Contract No. R804366-02. U.S. Environ. Prot. Agency.

Cooper, R.C., et al. 1979. Asbestos in domestic water supplies for five California counties. Part II, EHS Publ. No. 79-1, School of Public Health, Univ. Calif. Berkeley. p. 247.

Cooper, W.C. and J.L. Balzer. 1968. Evaluation and Control of Asbestos Exposures in the Insulating Trade. In: Holstein and Anspach (eds.), International Konferenz uber die Biologischen Wirkungen des Asbestos, Dresden, Germany, April 22-24. Berlin, Deutsche Zent. Arbeitsmed. p. 151.

Cooper, W.C. and J. Miedema. 1973. Asbestosis in the Manufacture of Insulating Materials. In: P. Bogovski, et al. (eds.), Biological Effects of Asbestos. IARC World Health Org., Lyon, France. p. 175.

Craun, G.F., et al. 1977. Exposure to Asbestos Fibers in Water Distribution Systems. In: Proc. 97th Ann. Conf. Am. Water Works Assoc., Anaheim, California, May 8-13.

Cunningham, H.M. and R.D. Pontefract. 1971. Asbestos fibers in beverages and drinking water. Nature. 232: 332.

Cunningham, H.M. and R.D. Pontefract. 1973. Asbestos fibers in beverages, drinking water and tissues: Their passage through the intestinal wall and movement through the body. Jour. Assoc. Off. Anal. Chem. 56: 976.

Cunningham, H.M. and R.D. Pontefract. 1974. Placental transfer of asbestos. Nature. 249: 177.

Cunningham, H.M., et al. 1976. Quantitative relationship of fecal asbestos to asbestos exposure. Jour. Toxicol. Environ. Health. 1: 377.

Cunningham, H.M., et al. 1977. Chronic effects of ingested asbestos in rats. Arch. Environ. Contam. Toxicol. 6: 507.

Davis, J.M.G., et al. 1978. Mass and number of fibers in the pathogenesis of asbestos-related lung disease in rats. Br. Jour. Can. 37: 673.

Doll, R. 1955. Mortality from lung cancer in asbestos workers. Br. Jour. Ind. Med. 12: 81.

Donna, A. 1970. Tumori sperimentali da amianto di crisotilo, crocidolite e amosite in ratto Sprague-Dawley. Med. Lavoro. 61: 1.

Duggan, M.J. and E.W. Culley. 1978. The counting of small numbers of asbestos fibers on membrane filters: A comparison of results from some commercial laboratories. Ann. Occup. Hyg. 21: 85.

Edge, J.R. 1976. Asbestos-related disease in Barrow and Furness. Environ. Res. 11: 244.

Edge, J.R. 1979. The incidence of carcinoma of the bronchus in shipyard workers with pleural plaques. Ann. N.Y. Acad. Sci. 330: 289.

Elmes, P.C. and M.J.C. Simpson. 1971. Insulation workers in Belfast. III. Mortality (1940-66). Br. Jour. Ind. Med. 28: 226.

Elmes, P.C. and M.J.C. Simpson. 1977. Insulation workers in Belfast. further study of mortality due to asbestos exposure (1940-75). Br. Jour. Ind. Med. 34: 174.

Enterline, P.E. and V. Henderson. 1973. Type of asbestos and respiratory cancer in the asbestos industry. Arch. Environ. Health. 27: 312.

Enterline, P., et al. 1972. Mortality in relation to occupational exposure in the asbestos industry. Jour. Occup. Med. 14: 897.

Evans, J.C., et al. 1973. Studies on the deposition of inhaled fibrous material in the respiratory tract of the rat and its subsequent clearance using radioactive tracer techniques. I. UICC crocidolite asbestos. Environ. Res. 6: 180.

Ferris, B.G., Jr., et al. 1971. Prevalence of chronic respiratory disease. Arch. Environ. Health. 23: 220.

Fleischer, W.E., et al. 1946. A health survey of pipe coverage operations in construction of naval vessels. Jour. Ind. Hyg. Toxicol. 28: 9.

Gibbs, G.W. and M. LaChance. 1974. Dust-fiber relationships in the Quebec chrysotile industry. Arch. Environ. Health. 28: 69.

Gibel, W., et al. 1976. Tierexperimentelle untersuchungen uber eine kanzerogene wirkung von asbestfiltermaterial nach oraler aufnahme. Arch. Geschwulstforsch. 46: 437.

Gillam, J.D., et al. 1976. Mortality patterns among hard rock gold miners exposed to an asbestiform mineral. Ann. N.Y. Acad. Sci. 271: 336.

Gloyne, S.R. 1935. Two cases of squamous carcinoma of the lung occurring in asbestosis. Tubercle. 17: 5.

Gross, P., et al. 1967. Experimental asbestosis: The development of lung cancer in rats with pulmonary deposits of chrysotile asbestos dust. Arch. Environ. Health. 15: 343.

Gross, P., et al. 1973. Lymphatic transport of fibrous dust from the lungs. Jour. Occup. Med. 15: 186.

Gross, P., et al. 1974. Ingested mineral fibers. Do they penetrate tissue or cause cancer? Arch. Environ. Health. 29: 341.

Hallenbeck, W.H., et al. 1978. Is chrysotile asbestos released from asbestos-cement pipe into drinking water? Jour. Am. Water Works Assoc. 70: 97.

Hammond, E.C., et al. 1979. Asbestos exposure, cigarette smoking, and death rates. Ann. N.Y. Acad. Sci. 330: 473.

Harington, J.S. 1962. Occurrence of oils containing 3,4-benzpyrene and related substances in asbestos. Nature. 193: 43.

Harington, J.S. and F.J.C. Roe. 1965. Studies of carcinogenesis of asbestos fibers and their natural oils. Ann. N.Y. Acad. Sci. 132: 439.

Harliss, K.W., et al. 1978. The acute effects of chrysotile asbestos exposure on lung function. Environ. Res. 16: 360.

Harries, P.G. 1968. Asbestos hazards in naval dockyards. Ann. Occup. Hyg. 11: 135.

Harries, P.G. 1971a. A comparison of mass and fibre concentrations of asbestos dust in shipyard insulation processess. Ann. Occup. Hyg. 14: 234.

Harries, P.G. 1971b. Asbestos dust concentrations in ship repairing: A practical approach to improving asbestos hygiene in naval dockyards. Ann. of Occup. Hyg. 14: 241.

Harries, P.G. 1976. Experience with asbestos disease and its control in Great Britain's naval dockyards. Environ. Res. 11: 261.

Harrington, J.M., et al. 1978. An investigation of the use of asbestos-cement pipe for public water supply and the incidence of gastrointestinal cancer in Connecticut, 1935-1973. Am. Jour. Epidemiol. 107: 96.

Henderson, V.I. and P.E. Enterline. 1979. Asbestos exposure: Factors associated with excess cancer and respiratory disease mortality. Ann. N.Y. Acad. Sci. 330: 117.

Holt, P.F., et al. 1964. The early effects of chrysotile asbestos dust on the rat lung. Jour. Pathol. Bacteriol. 87: 15.

Irwig, L.M., et al. 1979. Risk of asbestosis in crocidolite and amosite mines in South Africa. Ann. N.Y. Acad. Sci. (In press)

Jacobs, R., et al. 1978. Light and electron microscope studies of the rat digestive tract following prolonged and short-term ingestion of chrysotile asbestos. Br. Jour. Exp. Pathol. 59: 443.

Kay, G. 1973. Ontario intensifies search for asbestos in drinking water. Water Pollut. Control. 9: 33.

Kiviluoto, R. 1960. Pleural calcification as a roentgenologic sign of non-occupational endemic anthophyllite-asbestosis. Acta Radiol. Suppl. 194: 1.

Kleinfeld, M., et al. 1967. Mortality experience in a group of asbestos workers. Arch. Environ. Health. 15: 177.

Knox, J.F., et al. 1968. Mortality from lung cancer and other causes among workers in an asbestos textile factory. Br. Jour. Ind. Med. 25: 293.

Kogan, F.M., et al. 1972. The cancer mortality rate among workers of asbestos industry of the Urals. Gig. i Sanit. 37: 29.

Langer, A.M. 1974. Inorganic particles in human tissues and their association with neoplastic disease. Environ. Health Perspect. 9: 229.

Langer, A.M., et al. 1971. Chrysotile asbestos in the lungs of persons in New York City. Arch. Environ. Health. 22: 348.

Langer, A.M., et al. 1973. Identification of asbestos in human tissues. Jour. Occup. Med. 15: 287.

Langer, A.M., et al. 1978. Variation of some physical, chemical, and biological properties of chrysotile asbestos subjected to prolonged milling. Jour. Toxicol. Environ. Health. 4: 173.

LeFevre, M., et al. 1978. Accumulation of 2 µm latex particles in mouse Peyer's patches during chronic latex feeding. Experientia. 34: 120.

Levy, B.S., et al. 1976. Investigating possible effects of asbestos in city water: Surveillance of gastrointestinal cancer incidence in Duluth, Minn. Am. Jour. Epidemiol. 103: 362.

Lewinsohn, H.C. 1972. The medical surveillance of asbestos workers. R. Soc. Health Jour. 92: 69.

Lewis, B.G. 1977. Asbestos in cooling-tower waters. Argonne Natl. Lab., Argonne, Illinois. ANL/ES-63.

Lieben, J.P. and H. Pistawke. 1967. Mesothelioma and asbestos exposure. Arch. Environ. Health. 14: 559.

Lilis, R. and I.J. Selikoff. 1979. Asbestos disease in maintenance workers of the chemical industry. Ann. N.Y. Acad. Sci. 330: 127.

Lynch, J.R. and H.E. Ayer. 1966. Measurement of dust exposures in the asbestos textile industry. Jour. Am. Ind. Hyg. Assoc. 27: 431.

Lynch, J.R., et al. 1970. The interrelationships of selected asbestos exposure indices. Jour. Am. Ind. Hyg. Assoc. 31: 598.

Lynch, K.M. and W.A. Smith. 1935. Pulmonary asbestosis. III. Carcinoma of lung in asbestos-silicosis. Am. Jour. Cancer. 24: 56.

Lynch, K.M., et al. 1957. Pulmonary tumors in mice exposed to asbestos dust. Arch. Ind. Health. 15: 207.

Maltoni, C. and C. Annoscia. 1974. Mesotheliomas in Rats Following the Intraperitoneal Injection of Crocidolite. In: W. Davis and C. Maltoni (eds.), Advances in Tumour Prevention, Detection, and Characterization. Vol. 1: Characterization of Human Tumours. Excerpta Medica, Amsterdam. p. 115.

Mancuso, T.F. and E.J. Coulter. 1963. Methodology in industrial health studies. The cohort approach, with special reference to an asbestos company. Arch. Environ. Health. 6: 210.

Mason, T.J., et al. 1974. Asbestos-like fibers in Duluth water supply. Relation to cancer mortality. Jour. Am. Med. Assoc. 228: 1019.

McDonald, J.C. and D.K. Liddell. 1979. Mortality in Canadian miners and millers exposed to chrysotile. Ann. N.Y. Acad. Sci. 330: 1.

McDonald, J.C., et al. 1971. Mortality in the chrysotile asbestos mines and mills of Quebec. Arch. Environ. Health. 22: 677.

McDonald, J.C., et al. 1980. Dust exposure and mortality in chrysotile mining, 1910-75. Br. Jour. Ind. Med. 37: 11.

McEwen, J., et al. 1977. Mesothelioma in Scotland. Jour. Br. Med. 4: 575.

Merewether, E.R.A. 1947. Annual report of the chief inspector of factories for the year 1947. Her Majesty's Stationery Office, London.

Meurman, L.O., et al. 1974. Mortality and morbidity among the working population of anthophyllite asbestos miners in Finland. Br. Jour. Ind. Med. 31: 105.

Miller, L., et al. 1965. Tests for effect of asbestos on benzo(a)pyrene carcinogenesis in the respiratory tract. Ann. N.Y. Acad. Sci. 132: 489.

Millette, J.R. 1976. Analyzing for asbestos in drinking water. News of Environ. Res., Cincinnati, Ohio. Jan. 16.

Millette, J.R. 1979. Exposure to asbestos from drinking water in the United States EPA 600/1-79-150. Environmental Health Effects Research Report, Off. Res. Dev.

Millette, J.R., et al. 1979a. Aggressive water and water utilities from representative areas of the United States. Jour. Am. Water Works Assoc. (Submitted)

Millette, J.R., et al. 1979b. Concentration and size of asbestos in water supplies. Paper presented at NIEHS Workshop on the Biological Effects of Mineral Fibers and Particulates, Washington, D.C., June 7-8. (Submitted to Environ. Health Perspect.)

Morgan, A., et al. 1975. Studies on the deposition of inhaled fibrous material in the respiratory tract of the rat and its subsequent clearance using radioactive tracer techniques. II. Deposition of the UICC standard reference samples of asbestos. Environ. Res. 10: 196.

Mount Sinai. 1976. Rapport final cornite d'eltide seir la selubrite' daus l'indestive de l'amlante. Montreal, Canada. Annex.

Murphy, R.L.H., et al. 1971. Effects of low concentrations of asbestos. New England Jour. Med. 285: 1271.

Murray, H.M. 1907. Report of the departmental committee on compensation for industrial disease. Her Majesty's Stationery Office, London.

National Institute for Occupational Safety and Health. 1972. Criteria for a recommended standard: Occupational exposure to asbestos. HSM 72-10267. U.S. Government Printing Office, Washington, D.C.

National Institute for Occupational Safety and Health. 1976. Re-examination and update on the health effects of occupational exposure to asbestos. U.S. Government Printing Office, Washington, D.C.

Newhouse, M.L. 1969. A study of the mortality of workers in an asbestos factory. Br. Jour. Ind. Med. 26: 294.

Newhouse, M.L. and G. Berry. 1976. Predictions of mortality from mesothelial tumours in asbestos factory workers. Br. Jour. Ind. Med. 33: 147.

Newhouse, M.L. and G. Berry. 1979. Patterns of mortality in asbestos factory workers in London. Ann. N.Y. Acad. Sci. 330: 53.

Newhouse, M.L. and H. Thomson. 1965. Mesothelioma of pleura and peritoneum following exposure to asbestos in the London area. Br. Jour. Ind. Med. 22: 261.

Newhouse, M.L., et al. 1972. A study of the mortality of female asbestos workers. Br. Jour. Ind. Med. 29: 134.

Nicholson, W.J. 1971a. Measurement of asbestos in ambient air. Final report under Contract CPA 70-92. National Air Pollution Control Administration.

Nicholson, W.J. 1971b. Insulation hygiene progress reports 3: 2. Mount Sinai School of Medicine of the City University of New York.

Nicholson, W.J. 1974. Analysis of amphibole asbestiform fibers in municipal water supplies. Environ. Health Res. 9: 165.

Nicholson, W.J. 1976. Case study 1: Asbestos - the TLV approach. Ann. N.Y. Acad. Sci. 271: 152.

Nicholson, W.J. and F.L. Pundsack. 1973. Asbestos in the Environment. In: P. Bogovski, et al. (eds.), Biological Effects of Asbestos. IARC, Lyon, France. IARC Sci. Publ. No. 8. p. 126.

Nicholson, W.J., et al. 1971. Asbestos Air Pollution in New York City. In: H.M. England and W.T. Barry (eds.), Proc. Second Clean Air Cong. Academic Press, New York. p. 136.

Nicholson, W.J., et al. 1972. Asbestos contamination of parenteral drugs. Science. 177: 171.

Nicholson, W.J., et al. 1975. Asbestos contamination of the air in public buildings. Final report under Contract No. 68-02-1346. U.S. Environ. Prot. Agency.

Nicholson, W.J., et al. 1978. Control of sprayed asbestos surfaces in school buildings: A feasibility study under NIEHS Contract No. 1 ES-7-2113. Natl. Inst. Environ. Health Safety.

Nicholson, W.J., et al. 1979. Long-term mortality experience of chrysotile miners and millers in Thetford Mines, Quebec. Ann. N.Y. Acad. Sci. 330: 11.

Nicholson, W.J., et al. 1980a. Environmental Asbestos Concentrations in the United States. In: Proceedings of Conference on Asbestos and Mineral Fibers. IARC, Lyon, France.

Nicholson, W.J., et al. 1980b. Mortality experience of asbestos factory workers: Effect of differing intensities of asbestos exposure. Environ. Res. (In press)

Nordmann, M. and A. Sorge. 1941. Lungenkrebs durch asbeststaub im tierversuch. Z. Krebsforsch. 51: 168.

Nottle, M.C. 1977. Plant particles in kidneys and mesenteric lymph nodes of sheep. Aust. Vet. Jour. 53: 405.

Patel-Mandlik, K. and W. Hallenbeck. 1978. Fate of ingested chrysotile asbestos fiber in the newborn baboon. EPA 600/1-78 069. Report prepared for U.S. Environ. Prot. Agency.

Peto, J. 1978. The hygiene standard for asbestos. Lancet. 8062: 484.

Peto, J., et al. 1977. A mortality study among workers in an English asbestos factory. Br. Jour. Ind. Med. 34: 169.

Pontefract, R.D. and H.M. Cunningham. 1973. Penetration of asbestos through the digestive tract of rats. Nature. 243: 352.

Pooley, F.D. 1973. Mesothelioma in Relation to Exposure. In: P. Bogovski, et al. (eds.), Biological Effects of Asbestos. IARC, Lyon, France. IARC Sci. Publ. No. 8. p. 222.

Pott, F. and K.H. Friedrichs. 1972. Tumoren der ratte nach i.p.-injektion faserformiger staube. Naturwissenschaften. 59: 318.

Pott, F., et al. 1976. Ergebnisse aus tierversuchen zur kanzerogenen wirkung faserformiger staube und ihre deutung im hinblick auf die tumorentstehung beim menschen. Zbl. Bakt. Hyg., I Abt. Orig. B. 162: 467.

Pylev, L.N. and L.M. Shabad. 1973. Some Results of Experimental Studies in Asbestos Carcinogenesis. In: P. Bogovski, et al. (eds.), Biological Effects of Asbestos. IARC, Lyon, France. IARC. Sci. Publ. No. 8. p. 99.

Reeves, A.L. 1976. The carcinogenic effect of inhaled asbestos fibers. Ann. Clin. Lab. Sci. 6: 459.

Reeves, A.L., et al. 1971. Experimental asbestos carcinogenesis. Environ. Res. 4: 496.

Reeves, A.L., et al. 1974. Inhalation carcinogenesis from various forms of asbestos. Environ. Res. 8: 178.

Robinson, C., et al. 1979. Mortality Patterns, 1940-75, Among Workers Employed in an Asbestos Textile Friction and Packing Products Manufacturing Facility. *In*: R. Lemen and J.R. Dement (eds.), Dusts and Disease. Pathotox Publishers, Park Forest, Illinois. p. 131.

Rohl, A.N., et al. 1976. Asbestos exposure during brake lining maintenance and repair. Environ. Res. 12: 110.

Samudra, A., et al. 1978. Electron microscope measurements of airborne asbestos concentrations. A provisional methodology manual. Prepared under Contract No. 68-02-2251. EPA 600/2-77-178. U.S. Environ. Prot. Agency.

Sanders, E. and C.T. Ashworth. 1960. A study of particulate intestinal absorption and hepatocellular uptake. Exp. Cell Res. 22: 137.

Sawyer, R.N. 1977. Asbestos exposure in a Yale building: Analysis and resolution. Environ. Res. 13: 146.

Schnitzer, R.J., et al. 1971. Interaction of mineral fiber surfaces with cells *in vitro*. Ann. N.Y. Acad. Sci. 172: 747.

Schreiber, G. 1974. Ingested dyed cellulose in the blood and urine of man. Arch. Environ. Health. 29: 39.

Sebastien, P., et al. 1976. Les pollutions atmospheriques urbanies par l'asbeste. Rev. Franc. Mal. Resp. 4: 51.

Sebastien, P., et al. 1979. Translocation of Asbestos Fibers Through Respiratory Tract and Gastrointestinal Tract According to Fiber Type and Size. In: R. Lemen and J.R. Dement (eds.), Dusts and Disease. Pathotox Publishers, Park Forest, Illinois. p. 65.

Seidman, H., et al. 1979. Short-term asbestos work exposure and long-term observation. Ann. N.Y. Acad. Sci. 330: 61.

Selikoff, I.J. 1976. Lung cancer and mesothelioma during prospective surveillance of 1,249 asbestos insulation workers, 1963-1974. Ann. N.Y. Acad. Sci. 271: 448.

Selikoff, I.J., et al. 1964. Asbestos exposure and neoplasia. Jour. Am. Med. Assoc. 188: 22.

Selikoff, I.J., et al. 1965. The occurrence of asbestosis among insulation workers in the United States. Ann. N.Y. Acad. Sci. 132: 139.

Selikoff, I.J., et al. 1968. Asbestos exposure, smoking and neoplasia. Jour. Am. Med. Assoc. 204: 106.

Selikoff, I.J., et al. 1970. Mortality Experience of Asbestos Insulation Workers, 1943-68. In: M.A. Shapiro (ed.), Proc. Int. Conf. Pneumoconiosis, Johannesburg. Oxford Univ. Press, Capetown. p. 180.

Selikoff, I.J., et al. 1972. Carcinogenicity of amosite asbestos. Arch. Environ. Health. 25: 183.

Selikoff, I.J., et al. 1979a. Mortality experience of insulation workers in the United States and Canada, 1943-1977. Ann. N.Y. Acad. Sci. 330: 91.

Selikoff, I.J., et al. 1979b. Asbestos disease in United States shipyards. Ann. N.Y. Acad. Sci. 330: 295.

Shabad, L.M., et al. 1974. Experimental studies on asbestos carcinogenicity. Jour. Natl. Cancer Inst. 52: 1175.

Sincock, A.M. 1977. In vitro Chromosomal Effects of Asbestos and Other Materials. In: Origins of Human Cancer. Cold Spring Harbour, 1976.

Sincock, A. and M. Seabright. 1975. Induction of chromosome changes in Chinese hamster cells by exposure to asbestos fibers. Nature. 257: 56.

Smith, W.E. 1973. Asbestos, talc, and nitrates in relation to gastric cancer. Am. Ind. Hyg. Assoc. Jour. 33: 227.

Smith, W.E. and D.D. Hubert. 1974. The Intrapleural Route as a Means for Estimating Carcinogenicity. In: E. Karbe and J.F. Park (eds.), Experimental Lung Cancer. Springer-Verlag, Berlin. p. 92.

Smith, W.E., et al. 1965. Tests for carcinogenicity of asbestos. Ann. N.Y. Acad. Sci. 132: 456.

Smith, W.E., et al. 1970. An Experimental Model for Study of Cocarcinogenesis in the Respiratory Tract. In: P. Nettesheim, et al. (eds.), Morphology of Experimental Respiratory Carcinogenesis. U.S. Atomic Energy Comm., Oak Ridge, Tennessee. p. 299.

Stanton, M.F. 1973. Some Etiological Considerations of Fibre Carcinogenesis. In: P. Bogovski, et al. (eds.), Biological Effects of Asbestos. IARC, Lyon, France. IARC Sci. Publ. No. 8. p. 289.

Stanton, M.F. and C. Wrench. 1972. Mechanisms of mesothelioma induction with asbestos and fibrous glass. Jour. Natl. Cancer Inst. 48: 797.

Storeygard, A.R. and A.L. Brown. 1977. Penetration of the small intestinal mucosa by asbestos fibers. Mayo Clin. Proc. 52: 809.

Taskinen, E., et al. 1973. A current hypothesis of the lymphatic transport of inspired dust to the parietal pleura. Chest. 64: 193.

Thomson, J.G., et al. 1963. Asbestos as a modern urban hazard. S.A. Med. Jour. 37: 77.

Timbrell, V. 1965. The inhalation of fibrous dusts. Ann. N.Y. Acad. Sci. 132: 255.

U.S. EPA. 1974. A preliminary report on asbestos in the Duluth, Minnesota, area. Off. of Tech. Analysis. January.

U.S. EPA. 1976. Quarterly report of the Environmental Research Laboratory-Duluth, October-December, 1976. p. 5.

U.S. EPA. 1977. Comparison of ambient asbestos levels determined by various laboratories. Environ. Monitor. Support Lab. September.

Volkheimer, G. 1974. Passage of particles through the wall of the gastrointestinal tract. Environ. Health Perspect. 9: 215.

Wagner, J.C., et al. 1960. Diffuse pleural mesothelioma and asbestos exposure in the Northwestern Cape Province. Br. Jour. Ind. Med. 17: 260.

Wagner, J.C., et al. 1973. Mesotheliomata in rats after inoculation with asbestos and other materials. Br. Jour. Cancer. 28: 173.

Wagner, J.C., et al. 1974. The effects of inhalation of asbestos in rats. Br. Jour. Cancer 29: 252.

Wagner, J.C., et al. 1977a. Animal Experiments with Talc. In: W.C. Walton (ed.), Inhaled Particles and Vapors, IV. Pergamon Press, New York. (In press)

Wagner, J.C., et al. 1977b. Studies of the Carcinogenic Effect of Fibre Glass of Different Diameters Following Intrapleural Inoculation in Experimental Animals. In: Natl. Inst. Occup. Safety and Health Symp. Occup. Exposure to Fibrous Glass. Univ. of Maryland, 1977. (In press)

Wallingford, K.M. 1978. Chrysotile asbestos in industry. Paper presented to Natl. Inst. Occup. Safety and Health meeting, Washington Baltimore section of the Am. Ind. Hyg. Assoc., February.

Webster, I. 1970. Asbestos Exposure in South Africa. In: H.A. Shapiro (ed.), Pneumoconiosis Proc. of Int. Conf., Johannesburg. Oxford Univ. Press, Capetown. p. 209.

Weill, H., et al. 1979. Influence of dose and fiber type on respiratory malignancy risk in asbestos cement manufacturing. Am. Rev. Resp. Dis. 120: 345.

Weiss, A. 1953. Pleurakrebs bei lungenasbestose, in vivo morphologisch gesichert. Medizinische. 2: 93.

Weiss, W. 1971. Cigarette smoking, asbestosis and pulmonary fibrosis. Am. Rev. Resp. Dis. 104: 223.

Westlake, G.E., et al. 1965. Penetration of colonic mucosa by asbestos particles. An electron microscopic study in rats fed asbestos dust. Lab. Invest. 14: 2029.

Wigle, D.R. 1977. Cancer mortality in relation to asbestos in municipal water supplies. Arch. Environ. Health. 31: 185

Winer, A.A. and M. Cossette. 1979. The effect of aspect ratio on fiber counts: A preliminary study. Ann. N.Y. Acad. Sci. 330: 661.

Appendix I

Sample calculation of risk per 10^6 fibers/day ingested using a linear dose-response relationship.

$$\underset{A}{16.8 \times 10^{-2}} \times \underset{B}{\frac{1}{600(\text{f/ml})\ \text{yrs}}} \times \underset{C}{\frac{1}{8 \times 10^{6}\ \text{ml/day}}}$$

$$\times \underset{D}{\frac{1}{200}} \times \underset{E}{70\ \text{years}} \times \underset{F}{\frac{7}{5}} \times \underset{G}{10^{6}}$$

A = Percentage of excess GI cancer and peritoneal mesothelioma in study group.

B = Exposure index.

C = Exposure took place for 8 hours and the worker was assumed to breathe 1 m^3/hr (10^6 ml/hr).

D = Conversion from optical counts (fibers >5 μm) to electron microscopic counts (all fibers).

E = 70-year exposure to water is assumed.

F = Exposure was concentrated in 5 days rather than 7 days/week.

G = Calculation is for a 70-year risk per 10^6 fibers/day.

Appendix II

Sample calculation of risk per μg of asbestos ingested using a linear dose-response relationship.

$$\underset{A}{16.8 \times 10^{-2}} \times \underset{B}{\frac{1}{600(\mathrm{f/ml})\ \mathrm{yrs}}} \times \underset{C}{\frac{1}{8\ \mathrm{m^3/day}}} \times \underset{D}{\frac{.033\ \mathrm{f/ml}}{\mu\mathrm{g/m^3}}} \times \underset{E}{70\ \mathrm{years}} \times \underset{F}{\frac{7}{5}}$$

A = Percentage of excess GI cancer and peritoneal mesothelioma in study group.

B = Exposure index.

C = Exposure took place for 8 hours and the worker was assumed to breathe 1 m^3/hr.

D = Conversion of 30 μg/m^3 per 1 f/ml of chrysotile (Table 2).

E = 70-year exposure to water is assumed.

F = Exposure was concentrated in 5 days rather than 7 days/week.

Appendix III

Summary and Conclusions Regarding the Carcinogenicity of Asbestos*

Asbestos is a collective mineralogical term referring to naturally occurring minerals which have crystalized in the form of masses of long fibers which can be easily separated. This term also commonly refers to certain mineral occurrences in which fibrous silicate mineral can be extracted and used commercially for insulation, textiles, brake linings, asbestos cement, construction products, etc. Chrysotile, the fibrous form of serpentine, provides over 95 percent of the approximately 900,000 tons of asbestos consumed each year in the United States. The remaining asbestos used consists of the fibrous amphibole minerals crocidolite, amosite (fibrous grunerite), and anthophyllite. Fine dusts produced from the mining, milling, manufacturing, and use of these asbestos minerals contain discreet microscopic, elongated mineral particles of "fibers" which when inhaled by man are known to cause bronchogenic carcinoma and pleural and peritoneal mesothelioma.

Asbestos particles and other inorganic fibers introduced into the pleura, peritoneum, and trachea of rodents have induced malignant tumors in numerous studies reported in the literature. Limited and contradictory data exist for the carcinogenicity of asbestos administered to animals by ingestion. One study in which asbestos filter material was fed to rats (Gibel, et al. 1976) reports 12 malignant tumors in 42 exposed animals versus only 2 liver-cell carcinomas in 49 control animals. Electron microscope analysis of animal tissues for asbestos indicates that ingested fibers can accumulate at many sites following hematogenous or lymphatic transport of ingested fibers which pass through the gastrointestinal mucosa.

---

*This summary has been prepared and approved by the Carcinogens Assessment Group of EPA on June 23, 1979.

The strongest evidence for the carcinogenicity of ingested asbestos is provided by epidemiology of populations occupationally exposed to high concentrations of airborne asbestos dust. Inhalation exposure to asbestos dust is accompanied by ingestion exposure because high percentage of inhaled fibers are removed from the respiratory tract by mucociliary clearance and swallowed. Peritoneal mesothelioma, often in great excess since it is very rarely observed in the absence of asbestos exposure, and modest excesses of stomach, esophagus, colon-rectum, and kidney cancer have been observed associated with occupational exposure.

The influence of long-term chrysotile fiber contamination of San Francisco Bay area water supplies on cancer incidence has recently been studied by the University of California under an EPA grant. Significant dose response gradients for the incidence of several cancers, including white male lung and stomach and white female esophageal and peritoneal cancer, were noted independent of the effect of socioeconomic status. Other water supply studies are of limited value due to factors such as very low exposure and insufficient time elapsed since initial exposure of the population. Observation in human urine of mineral fibers previously ingested with drinking water has established that ingested asbestos can pass through the human gastrointestinal mucosa and migrate to various tissues.

Asbestos is a known carcinogen when inhaled. The demonstrated ability of asbestos to induce malignant tumors in different animal tissues, the passage of ingested fibers through the human gastrointestinal mucosa, and the extensive human epidemiological evidence for excess peritoneal, gastrointestinal, and other extrapulmonary cancer as a result of asbestos exposure suggests that asbestos is likely to be a human carcinogen when ingested.

The water quality criterion for asbestos particles is derived from the substantial data which exist for the increased incidence of peritoneal mesothelioma and gastrointestinal tract cancer in humans exposed occupationally to asbestos. This derivation assumes that much or all of this increased disease incidence is caused by fibers ingested following clearance from the respiratory tract. Several studies, including one of 17,800 insulation workers, allow the association of approximate air-borne fiber concentrations to which individuals were exposed with observed excess peritoneal and gastrointestinal cancer. All of the inhaled asbestos is assumed to be eventually cleared from the respiratory tract and ingested.

The water concentration, calculated to keep the individual lifetime cancer risk below 10^{-5}, is 300,000 fibers of all sizes/liter. The corresponding mass concentration for chrysotile asbestos is approximately 0.05 µg/liter.

Derivation of the Water Quality Criterion for Asbestos

The criterion for asbestos particles in water is derived from the substantial data which exist for the increased incidence of peritoneal mesothelioma and gastrointestinal tract cancer in humans exposed occupationally to asbestos. This derivation assumes that much or all of this increased disease incidence is caused by fibers ingested following clearance from the respiratory tract. Several studies, including one of 17,800 insulation workers, allow the association of approximate airborne fiber concentrations to which individuals were exposed with observed excess peritoneal and gastrointestinal cancer. All of the inhaled asbestos is assumed to be eventually cleared from the respiratory tract and ingested.

Excess deaths due to peritoneal mesothelioma and gastrointestinal cancer (ICD 150-158) equal approximately 12 percent of the expected number of deaths for asbestos workers in three different cohorts studied. An average exposure index of 430 years x fibers >5 μm/ml is calculated for these workers by multiplying average air fiber concentration estimates by average years of exposure time.

Since water measurement for asbestos requires electron microscope analysis for fibers (asbestos particles with length to width ratios ≥ 3.0) of all sizes, the occupational exposure index must be converted from fibers >5 μm (optical microscope) to fibers of all sizes (electron microscope). A ratio of 200 electron microscope identifiable fibers to one optical microscope identifiable fiber is used for chrysotile asbestos in workplace air samples. A much smaller ratio is expected for amphibole fibers.

Assuming a linear dose response, occupational exposure of 5 days/week and $8m^3$ air inhaled/workday, and 70 years for ingestion of drinking water, the criterion is calculated as follows:

$$\underset{A}{(430\ f>5\ \mu m/ml\ -\ years)}\ \underset{B}{(5/7)}\ \underset{C}{(200\ f/f>5\ \mu m)}\ \underset{D}{(1/70\ years)}$$

$$\underset{E}{(10^6 ml/m^3)}\ \underset{F}{(8m^3/day)}\ \underset{G}{(10^{-5}/1.2 \times 10^{-1})}$$

600,000 fibers of all sizes/day

A = Exposure index in years x fibers >5 μm/ml from Selikoff, et al. (1976, 1979a) and Newhouse and Berry (1979)

B = Occupational exposure for 5 days versus 7 days for water exposure.

C = Conversion from optical counts (F >5μm) to EM counts (all fibers) in fibers/fibers 5μm

D = 70-year exposure is assumed for drinking water.

E = Conversion from ml to m^3.

F = Occupational exposure for 8 hours while breathing $1m^3/1$ hour.

G = A risk of 10^{-5} is calculated from data on an average observed risk of 1.2×10^{-1} from Selikoff, et al. (1976, 1979a) and Newhouse and Berry (1979).

Based on these parameters and an average ingestion exposure of 2 liters of water per day, the water concentration calculated to keep the individual lifetime cancer risk below 10^{-5} is 300,000 fibers of all sizes/l. The corresponding mass concentration for chrysotile asbestos based on occupational data is approximately 0.05 µg/l.